Table 10: **RT**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
RT(1–5)	Pol(176–184)	TLNFPISPI	HIV-1 infection	human(A2 supertype)	[Propato (2001)]
	• Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)				
RT(3–12)	RT( )	SPIETVPVKL	HIV-1 infection	human(A2, B61)	[van der Burg (1997)]
	• Recognized by CTL from a long-term survivor, EILKEPVGHGV was also recognized • Highly conserved across clades				
RT(3–12)	Pol( )	SPIETVPVKL		human(B7)	[De Groot (2001)]
	• The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes • A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay • SPIETVPVKL was newly identified as HLA-B7 epitope in this study, it had been previously shown to be presented by HLA-A2 and B61				
RT(5–29)	RT(160–184 HXB2)	IETVPVKLKPGMDGP-KVKQWPLTEE	HIV-1 infection	human(B8)	[Walker (1989)]
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT(18–26)	RT(185–193)	GPKVKQWPL	HIV-1 infection	human(B8)	[Oxenius (2000)]
	• Epitope name: GPK. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable • Two of the 7/8 study subjects that were HLA B8+ recognized this epitope • Patient SC2 (HLA A1, B7/8, Cw0701/0702, DR4/53, DQ7) had CTL responses against epitopes FLKEKGGL, GPKVKQWPL, and GEIYKRWII – FLKEKGGL tetramer staining steadily declined and at day 1340 the FLKEKGGL stained cells were no longer detected and the escape mutant FLKENGGI was found in 8/10 clones • Patient SC11(HLA A1, B8, Cw0201, DR3/11, DR52, DQ2/7) started therapy early, remained on therapy for 40 days, then reinitiated HAART at day 640, and had a CTL response to FLKEKGGL, GPKVKQWPL, and GEIYKRWII throughout and received a benefit from the early limited course therapy				

RT(18–26)	RT(185–193 LAI)	GPKVKQWPL		human(B*0801)	[Brander & Goulder(2001)]
• C. Brander notes this is a B*0801 epitope					
RT(18–26)	RT(18–26)	GPKVKQWPL	HIV-1 infection	human(B8)	[Meier (1995), Menendez-Arias (1998)]
• HIV proteins with mutations in this epitope allowed transactive inhibition of specific CTL-mediated lysis • Article reviewed in [Menendez-Arias (1998)], with a discussion of antagonism					
RT(18–26)	RT(173–181)	GPKVKQWPL		human(B8)	[Goulder (1997g), Menendez-Arias (1998)]
• Included in a study of the B8 binding motif • Article reviewed in [Menendez-Arias (1998)], with a discussion of antagonism					
RT(18–26)	RT(185–193 LAI)	GPKVKQWPL		human(B8)	[Sutton (1993)]
• Predicted epitope based on B8-binding motifs, from larger peptide IETVPVKLKPGMDGPKVKQWPLTEE					
RT(18–26)	RT(185–193 LAI)	GPKVKQWPL	HIV-1 infection	human(B8)	[Klenerman (1995), Menendez-Arias (1998)]
• Naturally-occurring antagonist GPRVKQWPL found in viral PBMC DNA and RNA • Article reviewed in [Menendez-Arias (1998)] with a discussion of antagonism					
RT(18–26)	RT(18–26)	GPKVKQWPL	*in vitro* stimulation	human(B8)	[Zarling (1999)]
• This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL					
RT(18–26)	Pol( )	GPKVKQWPL	HIV-1 infection	human(B8)	[Seth (2001)]
• CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized					
RT(18–26)	RT(185–193 SF2)	GPKVKQWPL	HIV-1 infection	human(B8)	[Altfeld (2001c)]
• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection					

- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B8+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/3 group 2, and 2/2 group 3

RT(18–26)	Pol(171–180)	GPKVKQWPL	HIV-1 exposed seronegative, HIV-1 infection	human(B8)	[Kaul (2001a)]

- GPKVKQWPL is cross-reactive for clades A, B, C, and D
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

---

RT(18–26)	RT(18–26)	GPKVKQWPL	HIV-1 infection	human(B8)	[Day (2001)]

- B8-restricted CTL accounted for about 1/3 of the total CTL response in one individual

---

RT(18–27)	Pol( )	GPKVKQWPLT		human(B7,B8)	[De Groot (2001)]

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay
- GPKVKQWPLT was confirmed as a previously identified HLA-B8 epitope, and newly identified as an HLA-B7 epitope in this study

---

RT(33–41)	RT(33–41 LAI)	ALVEICTEM	HIV-1 infection	human(A*0201)	[Brander & Goulder(2001)]

- C. Brander notes this is an A*0201 epitope

RT(33–41)	RT(33–41 LAI)	ALVEICTEL	HIV-1 infection	human(A*0201)	[Samri (2000)]

- This epitope contains the mutation M41L, a mutation induced by nucleoside reverse transcriptase inhibitors
- Patient 201#5, (A*0201), was found by ELISPOT to recognize the mutated peptide after zidovudine treatment, but not the wild-type peptide – the mutation M41L gave an increased A2 binding score (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence
- Three additional A*0201 individuals and one B27 individual did not respond to this epitope before or after treatment
- M41L occurred at anchor positions p2 and p9 in several computer predicted RT epitopes (33-41, 32-41, and 40-49) (http//bimas.dcrt.nih.gov/molbio/hla_bind), and increased the predicted binding affinity for 6 HLA molecules (B*2705, B5102, C3, A0201, B*2705 and B3901)

RT(33–41)	RT(33–41)	ALVEICTEM	HIV-1 infection	human(A2)	[Haas (1998)]

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules

---

RT(33–41)	RT(33–41)	ALVEICTEM	HIV-1 infection	human(A2)	[Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person
- SLYNTVATL was the dominant A2 epitope recognized in patients with chronic infection, except for Subject 11841 who recognized 5/8 epitopes and who had a dominant A-2 response to ALVEICTEM

RT(33–43)	RT(33–43)	ALVEICTEMEK	HIV-1 infection	human(A*0301)	[Haas (1998)]

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules
- C. Brander notes that this is an A*0301 epitope in the 1999 database, G. Haas pers. comm.

RT(33–43)	RT(33–43)	ALVEICTEMEK	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]

- C. Brander notes this is an A*0301 epitope

RT(33–43)	RT(33–43)	ALVEICTEMEK	HIV-1 infection	human(A3)	[Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant

---

RT(38–52)	RT(203–209)	CTEMEKEGKISKIGP	Vaccine	murine(H-2^d)	[Burnett (2000)]

Vaccine: *Vector/type:* Salmonella *HIV component:* RT epitope

- A live attenuated bacterial vaccine, Salmonella SL3261-pHART, with an inserted HIV epitope in the Lpp-OmpA-HIV fusion protein, induced a specific CTL response in BALB/c mice (<15% lysis assayed by Cr-release of target cells)

RT(38–52)	RT(205–219 BRU)	CTEMEKEGKISKIGP	Vaccine	murine(H2^k)	[De Groot (1991), Menendez-Arias (1998)]

Vaccine: *Vector/type:* recombinant protein *Strain:* BRU *HIV component:* RT

- Murine and human helper and CTL epitope
- Epitope noted in a review by [Menendez-Arias (1998)] to be located in the “fingers” domain of RT and is a helper and CTL epitope

---

RT(38–52)	RT(205–219)	CTEMEKEGKISKIGP	HIV-1 infection	human(broad)	[Hosmalin (1990), Menendez-Arias (1998)]

- Murine and human helper and CTL epitope
- Epitope noted in a review by [Menendez-Arias (1998)] to be located in the "fingers" domain of RT and is a helper and CTL epitope

RT(39–47)	RT(206–214)	TEMEAEGKI	*in vitro* stimulation	C3H/HeJ mice( )	[Leggatt (1997)]

- Ala-substituted nonamer-peptide used to test a non-radioactive assay for murine CTL recognition of peptide-MHC class I complexes
- The new assay is CTL adherence assay (CAA), and is based on the discovery that CTL develop adhesive properties upon TCR triggering
- Substitutions in TEMEAEGKI that reduce cytolytic activity were correctly detected by CAA

RT(39–47)	RT( )	TEMEKEGKI		murine(H-2K^k)	[Leggatt (1998)]

- Epitope variants were examined for CTL response in concert with H-2K^k MHC class I binding – all of the following combinations were observed: (i) two single mutations which did not alone abrogate CTL activity did abrogate activity when combined, (ii) loss of recognition of a single substitution could be restored by an additional substitution, and (iii) sometimes there was recognition of two single substitutions as well as the combination of those substitutions
- 2E and 9I are anchor residues for H-2K^k – if you have M in the third position, it enhances H-2K^k binding 10-fold, but polymorphism at this site is important for the overall conformation of the peptide and can influence T-cell recognition

RT(42–50)	RT(42–50 LAI)	EKEGKISKI	HIV-1 infection	human(B*5101)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*5101 epitope

RT(42–50)	RT(42–50 LAI)	EKEGKISKI	HIV-1 infection	human(B51)	[Haas (1998)]

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules

RT(57–65)	Pol(236–244)	NTPVFAIKK	HIV-1 infection	human(A3 supertype)	[Propato (2001)]

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

RT(73–82)	RT(73–82 LAI)	KLVDFRELNK	HIV-1 infection	human(A3)	[Samri (2000)]

- This epitope contains the mutation L74V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors
- The wild-type, but not the mutated peptide, was recognized before and after zidovudine treatment in A3-restricted patients 252#0 and 252#4
- Mutation L74V affects the p2 anchor position in RT epitopes and was predicted to reduce binding to A3 (http://bimas.dcrt.nih.gov/molbio/hla_bind)

RT(93–101)	( )	GIPHPAGLK		(A3)	[Altfeld(2000), Brander & Goulder(2001)]
RT(93–102)	Pol(240–249 93TH253 CRF01)	GIPHPAGLKK	HIV-1 exposed seronegative	human(A11)	[Sriwanthana (2001)]

- Epitope name: P248-257. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was weakly reactive in the HEPS study subject 265 who was HLA A2/A11 and after a second stimulation *in vitro* gave a strong response in HEPS study subject 128 who was HLA A11/A33

RT(93–102)	Pol(240–249 93TH253 CRF01)	GIPHPAGLKK	HIV-1 infection	human(A11)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 2/8 tested FSWs recognized it
- This epitope was highly conserved in other subtypes, and exact matches were common

RT(98–113)	RT(252–266)	AGLKKKKSVTVLDVG-D	HIV-1 infection	human(Cw4)	[Bernard (1998)]

- This study focuses on six rare HIV-infected long-term survivors who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs

RT(103–117)	RT(257–251)	KKSVTVLDVGDAYFS	HIV-1 infection	human(Cw4)	[Bernard (1998)]

- This study focuses on six rare HIV-infected long-term survivors who were infected for many years without exhibiting immune
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs

RT(107–115)	RT(262–270 IIIB)	TVLDVGDAY		(B*3501)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*3501 epitope

RT(107–115)	RT(262–270 IIIB)	TVLDVGDAY	HIV-1 infection	human(B35)	[Menendez-Arias (1998), Wilson (1996)]

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study
- TVLDMGDAC is a naturally occurring variant that is less reactive
- [Menendez-Arias (1998)], in a review, notes that this epitope includes a catalytic residue (Asp-110) in the active site of RT

RT(107–115)	Pol(262–270 IIIB)	TVLDVGDAY	HIV-1 infection	human(B35)	[Wilson (1999a)]

- This study describes maternal CTL responses in the context of mother-to-infant transmission
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants
- An additional variant that gave a positive CTL response: TVLDMGDAC

RT(107–115)	Pol(262–270)	TVLDVGDAY	HIV-1 infection	human(B35)	[Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

---

RT(107–115)	RT(262–270 SF2)	TVLDVGDAY	HIV-1 infection	human(B35)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 0/1 group 3

RT(108–118)	RT(267–277)	VLDVGDAYFSV	*in vitro* stimulation	human(A*0201)	[van der Burg (1996)]

- High dissociation rate, but immunogenic in primary CTL induction after repeated stimulations with peptide
- CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual

---

RT(108–118)	RT(267–277)	VLDVGDAYFSV	HIV-1 infection	human(A2)	[Kundu (1998b)]

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated
- VLDVGDAYFSV is a conserved HLA-A2 epitope included in this study – 4/6 patients had this sequence as their HIV direct sequence, but only one of these had a detectable CTL response – the other two had the sequences EEDVGDAYFSV and ELDVGDAYFSV and no detectable CTL response

---

RT(108–118)	RT(267–277)	VLDVGDAYFSV	*in vitro* stimulation	human(A2)	[van der Burg (1995)]

- Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor
- VLDVGDAYFSV is in a functional domain

RT(108–118)	Pol(263–273)	VLDVGDAYFSV	HIV-1 infection	human(A2, A*0201)	[Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

---

RT(108–122)	RT(257–251)	VLDVGDAYFSVPLDE	HIV-1 infection	human(Cw4)	[Bernard (1998)]

- This study focuses on six rare HIV-infected long-term survivors who were infected for many years without exhibiting immune dysregulation – such immunologically normal HIV-infected (INHI) cases occur at a frequency between 0.1 and 1% in the infected population
- No direct CTL were found in any of the six INHIs, but above background CTLp activity was founded in 3/6 INHIs

---

RT(113–120)	Pol(268–275 SF2)	DAYFSVPL	HIV-1 infection	human(B*5101, B24)	[Tomiyama (1999)]

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA -B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed
- Four of the six epitopes were highly conserved among B subtype sequences, DAYFSVPL is conserved

---

RT(117–126)	Pol(264–273 93TH253 CRF01)	SVPLDESFRK	HIV-1 exposed seronegative	human(A11)	[Sriwanthana (2001)]

- Epitope name: P272-281. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope after a second stimulation *in vitro* gave a strong response in HEPS study subject 128 who was HLA A11/A33

RT(117–126)	Pol(264–273 93TH253 CRF01)	SVPLDESFRK	HIV-1 infection	human(A11)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 3/8 tested FSWs recognized it
- This epitope was only conserved in CRF01, and subtype A and B, and exact matches were uncommon

---

RT(118–126)	Pol(273–282)	VPLDKDFRKY	HIV-1 infection	human(B*3501)	[Tomiyama (2000a)]

- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

RT(118–126)	( )	VPLDEDFRKY	HIV-1 infection	human(B*3501)	[Tomiyama (2000b)]

- Epitope name: HIV-B3501-SF2-4. B*3501-VPLDEDFRKY tetramer binding did not inhibit CTL activity of a clone that reacts with both HLA-B*3501 and HLA-B*5101 presentation of the epitope IPLTEEAEL

RT(118–126)	RT(273–282 SF2)	VPLDEDFRKY	HIV-1 infection	human(B35)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 1/1 group 3

RT(118–127)	RT(273–282 SF2)	VPLDKDFRKY	HIV-1 infection	human(B*3501)	[Menendez-Arias (1998), Tomiyama (1997)]

- A CTL clone responsive to this epitope was obtained
- 4/7 B35-positive individuals had a CTL response to this epitope
- A K to E substitution at position 5 abrogates specific lysis, and reduces binding to B*3501
- [Menendez-Arias (1998)], in a review, notes that a Glu to Lys (E to K) change abrogates CTL activity, but that both VPLDEDFRKY and VPLDKDFRKY can serve as HLA-B35 epitopes, so the change must alter T-cell receptor binding – residues in this epitope may be important for polymerase activity

---

RT(118–127)	RT(273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human(B*3501)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*3501 epitope

RT(118–127)	RT(273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human(B*3501,B35)	[Shiga (1996)]

- Binds HLA-B*3501

RT(118–127)	( )	VPLDKDFRKY	HIV-1 infection	human(B35)	[Kawana (1999)]

- HLA B35 is associated with rapid disease progression
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation
- `-----E----` was found in 8/10 of the B35+ individuals, and three of the B35- individuals – the D –> E substituted peptide had similar binding affinity to B35 and was equally susceptible to a CTL clone

---

RT(118–127)	RT(273–282 IIIB)	VPLDEDFRKY	HIV-1 infection	human(B35)	[Sipsas (1997)]

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by three lab workers accidentally infected with HIV-1 IIIB

- VPLDKDFRKY, a variant found in HIV MN, was not recognized
- VPHDEDFRKY, a variant found in HIV YU2, was not recognized
- This epitope was type-specific and conserved in only one other B subtype sequence

---

RT(126–135) RT(293–302 HXB) KYTAFTIPSI HIV-1 infection human(A2) [Shankar (1998)]

- A novel CTL clone was defined with a panel of recombinant vaccinia-RT-infected B-LCL target cells using PBMCs donated by a patient who was HIV-seropositive for 6 years and had not received any antiretroviral therapy
- There is evidence that some CTL epitopes are poorly presented on the surface of infected cells, but this RT epitope was recognized as effectively on HIV-infected cells as on peptide-pulsed targets

---

RT(127–135) Pol( ) YTAFTIPSI HIV-1 infection human(A2) [Altfeld (2001d)]

- Epitope name: Pol-316. HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested
- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acutely infected individuals recognized at least 1 (median of 1 and maximum of 2)
- 2/22 individuals with chronic HIV-1 infection recognized this epitope in ELISPOT
- 0/12 acutely infected individuals recognized this epitope
- YTAFTIPSI binds to five HLA-A2 supertype alleles: A*0201, A*0202, A*0203, A*0206 and A*6802 (highest affinity)

RT(127–135) Pol(306–314) YTAFTIPSI HIV-1 infection human(A2 supertype) [Propato (2001)]

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind five HLA-A2 supertypes alleles (A*0201, A*0202, A*0203, A*0206 and A*6802)

RT(128–135) Pol(283–290 HXB2) TAFTIPSI HIV-1 infection human(A*0217) [Mulligan (2001)]

- Epitope P28 from Patient 12129 with HLA genotypes A*0207, A*0217, B*0801, B*4002, Cw*0303, Cw*07(01, 06)

RT(128–135) RT(295–302 IIIB) TAFTIPSI HIV-1 infection human(B*5101) [Brander & Goulder(2001)]

- C. Brander notes this is a B*5101 epitope

RT(128–135) Pol(283–290 SF2) TAFTIPSI HIV-1 infection human(B*5101) [Tomiyama (1999)]

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS, while HLA-B35, -B8, -B24 are associated with a rapid progression to AIDS (Nat. Med. 2:405, 1996;Lancet 22:1187, 1986;Hum Immunol 22:73, 1988;Hum Immunol 44:156, 1995)
- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%

- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed
- Four of the six epitopes were highly conserved among B subtype sequences, but TAFTIPSI is somewhat variable

---

RT(128–135) RT(295–302) TAFTIPSI HIV-1 infection human(B*5101) [Samri (2000)]

- Epitope name: P5. The epitope TAFTIPSI was recognized by patient 246#1 in a study of the effects of therapy escape mutations on CTL recognition

---

RT(128–135) RT(295–302 IIIB) TAFTIPSI HIV-1 infection human(B51) [Menendez-Arias (1998), Sipsas (1997)]

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB
- TAFTIPST, a variant found in HIV-1 CAM1, was also recognized but 100-fold more peptide was needed
- TAFTIPSV, a variant found in HIV-1 VE1RT, was also recognized, but 10-fold more peptide was needed
- TVFTIPSI, a variant found in HIV-1 MANC, was also recognized
- [Menendez-Arias (1998)], in a review, notes that this epitope includes a region near the active site of RT – the substitution of the position two conservative change from A to V decreases CTL recognition

---

RT(128–135) RT(295–302) TAFTIPSI HIV-1 infection human(B51) [Betts (2000)]

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant
- Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes
- Three of the four individuals that responded to SLYNTVATL recognized additional HIV epitopes, and all three were also HLA B51 and recognized this epitope as well as other epitopes

---

RT(128–135) RT(295–302) TAFTIPSI HIV-1 infection human(B51) [Oxenius (2000)]

- Epitope name: TAF. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable
- None of the 8 study subjects recognized this epitope but none were HLA B51+

RT(128–135) RT(295–302 LAI) TAFTIPSI HIV-1 infection human(B51) [Mollet (2000)]

- Epitope name: P5. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change

---

RT(151–159) Pol(306–314 SF2) QGWKGSPAI HIV-1 infection human(B*5101) [Tomiyama (1999)]

- HLA-B27, -B51, and -B57 are associated with slow progression to AIDS

- 15% of Japanese populations carry HLA-B51 while HLA-B27 and -B57 are detected in less than 0.3%
- Of the 172 HIV-1 peptides with HLA-B*5101 anchor residues, 33 bound to HLA-B*5101, seven of these peptides were reactive with CTL from 3 B*5101 positive individuals, and six were properly processed
- Four of the six epitopes were highly conserved among B subtype sequences, QGWKGSPAI is conserved

---

RT(153–165) RT(308–320) WKGSPAIFQSSMT HIV-1 infection human(B7) [Brander & Walker(1995)]

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study

---

RT(153–165) Pol(308–320) WKGPAIFQSSMT HIV-1 infection human(B7) [Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

---

RT(153–167) RT( ) WKGSPAIFQSSMTKI HIV-1 infection human( ) [Altfeld (2001a)]

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses is underestimated if accessory proteins are not included in the study
- RT peptides SQIYPGIKVRQLCKL and WKGSPAIFQSSMTKI were recognized

---

RT(156–164) RT(311–319 SF2) SPAIFQSSM HIV-1 infection human(B*3501) [Menendez-Arias (1998), Tomiyama (1997)]

- A CTL clone responsive to this epitope was obtained
- Only 1/7 B35-positive individuals had a CTL response to this epitope
- [Menendez-Arias (1998)], in a review, notes that this epitope is near the active site of RT

RT(156–164) RT(311–319 SF2) SPAIFQSSM HIV-1 infection human(B35) [Menendez-Arias (1998), Shiga (1996)]

- Binds HLA-B*3501
- [Menendez-Arias (1998)], in a review, notes that this epitope includes catalytic residues in the active site of RT

RT(156–164) Pol(311–319) SPAIFQSSM HIV-1 infection human(B35) [Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

---

RT(156–164) Pol(156–164 HXB2) SPAIFQSSM HIV-1 infection human(B7) [Hay (1999)]

- CTL response to IPRRIRQGL was the immunodominant response in a rapid progressor – there was a subdominant response to SPAIFQSSM in Pol, and interestingly, no response to commonly immunodominant HLA A*0201 epitope SLYNTVATL, although this individual was HLA A*0201
- The individual showed a strong initial CTL response at the time of the initial drop in viremia, but it was quickly lost, although memory cells persisted
- Despite the initial narrow response to two epitopes, no other CTL responses developed

- No HIV-specific lymphoproliferative responses were detected in this patient, and neutralizing antibody response was weak
- Variants of this epitope were observed *in vivo* (`------C--`, `--S------`), but the binding motifs for B7 were preserved (P2, and C-term aromatic or hydrophobic)

RT(156–164) Pol( ) SPAIFQSSM HIV-1 infection human(B7) [Islam (2001)]

- Subject 053i was followed longitudinally from acute infection through death, and had rapid progression to AIDS
- This individual had a dominant response to IPRRIRQGL with strong *in vivo* activated responses and *in vitro* stimulated memory responses and a subdominant response to SPAIFQSSM – during the course of disease progression (4 Years), the functional CTL responses were lost and no sequence variation occurred within both epitopes, but CTL clones specific for IPRRIRQGL persisted throughout

---

RT(156–164) RT(323–331 SF2) SPAIFQSSM HIV-1 infection human(B7) [Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B7+ individuals that had a CTL response to this epitope broken down by group: 0/4 group 1, 0/3 group 2, and 1/1 group 3

RT(156–165) RT(311–319 LAI) SPAIFQSSMT HIV-1 infection human(B35) [Samri (2000)]

- Epitope name: P4. This epitope contains the mutation P157S which can be induced by nucleoside reverse transcriptase inhibitors
- It was recognized by patient 252#0 in a study of the effects of therapy escape mutations on CTL recognition

---

RT(156–165) RT(311–319 SF2) SPAIFQSSMT human(B7) [Brander & Walker(1997), Menendez-Arias (1998)]

- Pers. Comm. from C. Hey and D. Ruhl to C. Brander and B. Walker
- [Menendez-Arias (1998)], in a review, notes that this epitope includes catalytic residues in the active site of RT

RT(156–165) RT(311–319 SF2) SPAIFQSSMT HIV-1 infection human(B7) [Mollet (2000)]

- Epitope name: P4. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change

---

RT(156–165) Pol( ) SPAIFQSSMT human(B7) [De Groot (2001)]

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes

- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay
- SPAIFQSSMT was confirmed as a previously identified HLA-B7 epitope in this study

RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	HIV-1 infection	human(A*0301)	[Brander & Goulder(2001)]

- C. Brander notes this is an A*0301 epitope

RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]

- C. Brander notes this is an A*1101 epitope

RT(158–166)	RT(325–333)	AIFQSSMTK	HIV-1 infection	human(A*1101, A3, A*0301, A*6801)	[Menendez-Arias (1998), Threlkeld (1997)]

- Study of the fine specificity of an A3-like super-type epitope (the A3 super-type includes A*0301, A*1101, A*3101, A*3301, and A*6801)
- A3 super-type is characterized by a hydrophobic or hydroxyl containing anchor residue at position 2, and a positive charge in the C-term position
- While most lines were specific, promiscuous cloned CTL lines were also derived from HIV+ donors that could recognize epitope presented by either A3 or A11 or A*6801
- Alanine substitutions throughout the epitope and natural variants indicate that the same amino acid positions are critical for presentation by either MHC molecule, A3 or A11
- AIFQSSMTK is presented by three members of the A3 superfamily: A*0301, A*1101, and A*6801, and the naturally occurring variants A1S and K9R are recognized with similar efficiency to wild type epitope – AIFQRSMTR can also bind to two additional members of the A3 superfamily, A*3101 and A*3301

RT(158–166)	RT( )	AIFQSSMTK	HIV-1 infection	human(A11)	[Wagner (1998a)]

- CTL specific for HIV epitopes were used to show that the mediators of both the cytolytic (granzyme A was used as the marker) and non-cytolytic (HIV-1 inhibitory chemokines MIP-1 α and RANTES were used as markers) anti-viral responses are localized within the CTL's cytotoxic granules

RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	Peptide-HLA interaction	human(A11)	[Menendez-Arias (1998), Zhang (1993)]

- Exploration of A11 binding motif, based on Nixon *et al.* 1991

RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	HIV-1 infection	human(A11)	[McMichael & Walker(1994)]

- Review of HIV CTL epitopes

RT(158–166)	Pol(305–313 93TH253 CRF01)	AIFQSSMTK	HIV-1 exposed seronegative, HIV-1 infection	human(A11)	[Sriwanthana (2001)]

- Epitope name: P313-321. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand

- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33
- This epitope was strongly reactive in HIV+ study subjects 053 and 184 who carried HLA-A11

RT(158–166) Pol(305–313 93TH253 CRF01) AIFQSSMTK HIV-1 infection human(A11) [Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified
- This epitope was predicted by the EpiMatrix method to be likely to bind to A11, and it served as an epitope in the FSWs, it was one of the six A11 epitopes that had been previously defined
- 6/8 tested FSWs recognized this epitope
- An HLA-A11 tetramer was made for this epitope, which was recognized by two subjects – and both subjects had expanded tetramer staining T-cell populations after *in vitro* stimulation
- This epitope was highly conserved in other subtypes, and exact matches were common

---

RT(158–166) RT(325–333 IIIB) AIFQSSMTK HIV-1 infection human(A3) [Wilson (1996)]

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study
- AIFQSSMTR and AILQSSMTK, naturally occurring variants, were found in the infant, and are recognized
- TISQSSMTK, a naturally occurring variant, was found in the infant and is not recognized

---

RT(158–166) RT(325–333 LAI) AIFQSSMTK HIV-1 infection human(A3) [Cao (1997)]

- The consensus peptide of B and D clade viruses is AIFQSSMTK
- The consensus peptide of a subset of As is AIFQASMTK and it is less able to stimulate the CTL clone
- The consensus peptide of a subset of As is SIFQSSMTK and is as reactive as the originally defined epitope

---

RT(158–166) Pol(325–333 IIIB) AIFQSSMTK HIV-1 infection human(A3) [Wilson (1999a)]

- This study describes maternal CTL responses in the context of mother-to-infant transmission
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants
- One variant found in an infant gave a positive CTL response: AIFQSSMTR
- AIFLSSMTK and TISQSSMTK were escape mutants

RT(158–166) RT(325–333 SF2) AIFQSSMTK HIV-1 infection human(A3) [Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection

- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-A3+ individuals that had a CTL response to this epitope broken down by group: 0/7 group 1, 0/4 group 2, and 1/2 group 3

RT(158–166) RT(158–166) AIFQSSMTK HIV-1 infection human(A3) [Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant
- In two of the subjects, AIFQSSMTK was the dominant epitope

RT(158–166) Pol(337–345) AIFQSSMTK HIV-1 infection human(A3 supertype) [Propato (2001)]

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 3/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

RT(158–166) Pol(313–321) AIFQSSMTK HIV-1 infection human(A3, A11) [Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

---

RT(158–166) RT(325–333) AIFQSSMTK HIV-1 infection human(A3.1) [Brander & Walker(1995)]

- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study

---

RT(158–166) RT(325–333) AIFQSSMTK HIV-1 infection human(A3.1) [Betts (2000)]

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant
- Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes
- 1/11 of the A2+ individuals was HLA A3 and reacted with this epitope as well as two other A3.1 epitopes

---

RT(158–166) RT(325–333 LAI) AIFQSSMTK human(A33) [Rowland-Jones(1995)]

- Defined as minimal peptide by titration curve, S. Rowland-Jones, Pers. Comm.

RT(158–166)	( )	AIFQSSMTK	HIV-1 infection	human(A33)	[Kaul (2001b)]

- This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative
- The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire
- This epitope was recognized in 1/22 HEPS sex worker controls, ML1668

RT(158–166)	RT(325–333 LAI)	AIFQSSMTK	HIV-1 infection	human(A3supertype)	[Mollet (2000)]

- Epitope name: P3. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using CD8+ cell IFNγ production to measure responses
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change

---

RT(158–166)	( )	AIFQSSMTK	HIV-1 infection	human(B*0301)	[Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and was appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

RT(158–166)	Pol(325–333)	AIFQSSMTK	HIV-1 exposed seronegative, HIV-1 infection	human(A3, A11, A33)	[Kaul (2001a)]

- Variants (S/A)IFQSSMTK are specific for the A/B clades
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women

- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure
- Among HLA-A3 women, 2/2 HEPS and 3/3 HIV-1-infected women recognized this epitope
- The dominant response to this HLA allele was to this epitope in one of the 2/2 HEPS cases and in one of the 3/3 HIV-1-infected women

RT(158–182)	RT(325–349 PV22)	AIFQSSMTKILEPFRKQ-NPDIVIYQ	HIV-1 infection	human(A11)	[Jassoy (1993)]

- HIV-1 specific CTLs release γ-IFN, and α- and β-TNF

RT(158–182)	RT(325–349)	AIFQSSMTKILEPFRKQ-NPDIVIYQ	HIV-1 infection	human(A11)	[Price (1995)]

- Study of cytokines released by HIV-1 specific activated CTL

RT(164–172)	Pol(343–351)	MTKILEPFR	HIV-1 infection	human(A3 supertype)	[Propato (2001)]

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind 4/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)

RT(173–181)	RT(173–181 LAI)	KQNPDIVIY		human(A*3002)	[Brander & Goulder(2001), Goulder (2001b)]

- C. Brander notes this is an A*3002 epitope

RT(173–181)	RT( )	KQNPDIVIY	HIV-1 infection	human(A*3002)	[Goulder (2001a)]

- Epitope name: KY9 (RT-53). HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule
- A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood
- Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean
- In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant
- In subject 199 four additional A*3002 epitopes were identified
- Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)

RT(175–183)	Pol( )	HPDIVIYQY	HIV-1 infection	human(B35)	[Kaul (2001b)]

- This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative
- HPDIVIYQY or NPDIVIYQY was recognized in 1 of the 6 women (ML857), and the response was present in the last available sample prior to seroconversion, 7 months
- 20/20 sequences of the infecting strain had three substitutions in this epitope, all 20 were NpQiIiyqy, and this form was not recognized by CTL from ML 857 – this was the only case in the study where a virus carrying an unrecognized form of the epitope broke through
- The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire
- NPDIVIYQY was recognized by 1/22 HEPS control sex workers, ML887

RT(175–183) RT(328–336 IIIB) NPDIVIYQY HIV-1 infection human(B*3501) [Tomiyama (1997)]

- A CTL clone responsive to this epitope was obtained
- 3/7 B35-positive individuals had a CTL response to this epitope
- D to E, or V to I, substitutions at positions 3 or 5, respectively, reduces CTL activity and binding to B*3501

RT(175–183) RT(328–336 IIIB) NPDIVIYQY HIV-1 infection human(B*3501) [Brander & Goulder(2001)]

- C. Brander notes this is a B*3501 epitope

RT(175–183) RT(342–350 LAI) HPDIVIYQY HIV-1 infection human(B*3501) [Brander & Goulder(2001)]

- C. Brander notes this is a B*3501 epitope

RT(175–183) Pol(330–338) NPDIVIYQY HIV-1 infection human(B*3501) [Tomiyama (2000a)]

- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

RT(175–183) RT(342–350 LAI) HPDIVIYQY HIV-1 infection human(B35) [McMichael & Walker(1994)]

- Review of HIV CTL epitopes

RT(175–183) RT(329–337) HPDIVIYQY HIV-1 infection human(B35) [Rowland-Jones (1995)]

- NPDIVIYQY preferred sequence for some CTL clones, HIV-2 NPDVILIQY is also recognized

---

RT(175–183) ( ) NPDIVIYQY HIV-1 infection human(B35) [Kawana (1999)]

- HLA B35 is associated with rapid disease progression
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals

- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals – only one of these reduced the binding of the peptide to B35 and was shown to be an escape mutation
- `--E------` was found in 8/10 of the B35+ individuals, and two of the B35- individuals – the D –> E substituted peptide had reduced binding affinity to B35 and may be an escape mutant

RT(175–183)	RT(329–337)	HPDIVIYQY	*in vitro* stimulation	human(B35)	[Lalvani (1997)]

- A peptide-based protocol was optimized for restimulation of CTLp using optimized peptide and IL-7 concentrations – importantly this protocol does not stimulate a primary response, only secondary – peptide-specific CTLp counts could be obtained via staining with peptide-Class I tetramers
- This peptide was one of the B35 presented test peptides used in control experiments showing that the assay gave no activity using lymphocytes from 21 healthy B35 seronegative donors

RT(175–183)	RT(328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human(B35)	[Menendez-Arias (1998), Shiga (1996)]

- Binds HLA-B*3501
- CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding [Menendez-Arias (1998)]

RT(175–183)	RT(328–336 IIIB)	NPDIVIYQY	HIV-1 infection	human(B35)	[Menendez-Arias (1998), Sipsas (1997)]

- HIV IIIB proteins were used to define the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB
- NPDIIIYQY, a variant found in HIV-1 JRCSF, was also recognized
- NPEIVIYQY, was also recognized
- NPDLVIYQY, was also recognized
- [Menendez-Arias (1998)], in a review, notes that the YXDD motif, highly conserved among polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding

RT(175–183)	RT( )	NPDIVIYQY	HIV-1 exposed seronegative	human(B35)	[Menendez-Arias (1998), Rowland-Jones (1998a)]

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating
- The A subtype consensus is HPDIVIYQY
- The D subtype consensus is NPEIVIYQY
- [Menendez-Arias (1998)], in a review, notes that the YXDD motif, highly conserved among polymerases, overlaps this epitope – CTL activity to this epitope was originally detected in a long-term survivor, however it has since been found in normal progressors – it is cross-reactive with HIV-2 (HPDILIYQY), but D3E and V5I substitutions reduce binding

RT(175–183)	Pol( )	NPDIVIYQY	HIV-1 exposed seronegative	human(B35)	[Rowland-Jones (1998b)]

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes
- Clade A version of epitope HPDIVIYQY, clade D NPEIVIYQY

RT(175–183) Pol( ) HPDIVIYQY human(B35) [Rowland-Jones (1999)]

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no δ32 deletion in CCR5
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective
- HIV-2 version of this epitope is not conserved: NPDVILIQY, but the CTLs are cross-reactive – one of five B35 CTL epitopes that are cross-reactive, see also [Rowland-Jones (1995)]

RT(175–183) ( ) HPDIVIYQY HIV-1 infection human(B35) [Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and was appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

RT(175–183) Pol(342–350) HPDIVIYQY HIV-1 exposed seronegative, HIV-1 infection human(B35) [Kaul (2001a)]

- Variants (H/N)PDIVIYQY are specific for the A/B clades
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure
- Among HLA-B35 women, 2/3 HEPS and 1/4 HIV-1-infected women recognized this epitope

- The dominant response to this HLA allele was to this epitope in only one of the 2/3 HEPS cases, and was not to this epitope in the one responsive HIV-1-infected women
- Subject ML 857 shifted from an A*6802 DTVLEDINL and B35 H/NPDIVIYQY response prior to seroconversion to a B35 PPIPVGDIY and B35 VPLRPMTY response post-seroconversion and the loss of the pre-seroconversion response was not due to sequence variation within these epitopes

RT(175–184)	RT(175–184 LAI)	NPDIVIYQYM	HIV-1 infection	human(B51)	[Samri (2000)]

- This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors
- Patient 246#1 (B51), was found by ELISPOT to recognize the wild type and the mutated peptide after zidovudine treatment
- The resistance mutation M184V gave an increased predicted binding score to B51 (http://bimas.dcrt.nih.gov/molbio/hla_bind) compared to the wildtype RT sequence and also an increased ELISPOT reactivity

RT(175–199)	RT(342–366 LAI)	NPDIVIYQYMDDLYV-GSDLEIGQHR	HIV-1 infection	human(A11)	[Menendez-Arias (1998), Walker (1989)]

- One of five epitopes defined for RT-specific CTL clones in this study

RT(179–187)	RT( )	VIYQYMDDL	Vaccine	human(A*0201)	[Hanke (1998a), Hanke (1998b)]

Vaccine: *Vector/type:* vaccinia *HIV component:* polyepitope

- This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans

RT(179–187)	RT( )	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Tan (1999)]

- Adoptive transfer of two autologous *in vitro*-expanded CTL clones against the A*0201 restricted epitopes SLYNTVATL and VIYQYMDDL were infused into a patient – they were well tolerated, but the SLYNTVATL clone was shown by tetramer staining to be rapidly eliminated through apoptosis, and the treatment had no impact upon viral load and CD4 and CD8 cell counts
- Tetramer staining failed for the VIYQYMDDL epitope as the tetramer was unstable

RT(179–187)	Pol(346–354)	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Sewell (1999)]

- Proteasome regulation influences epitope processing and could influence patterns of immunodominance
- The proteasome is inhibited by lactacystin treatment, and γ IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome
- IFN-γ induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways
- ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway
- This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants

RT(179–187)	RT(346–354 LAI)	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Harrer (1996a), Menendez-Arias (1998)]

- The substitution VIYQYVDDL abrogates CTL response and confers drug resistance
- [Menendez-Arias (1998)], in a review, notes that this epitope includes catalytic residues (Asp-185 and Asp-186) in the active site of RT

RT(179–187)	RT(346–354 LAI)	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Brander & Goulder(2001)]

- C. Brander notes this is an A*0201 epitope

RT(179–187)	RT(346–354)	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Brander (1998), Menendez-Arias (1998)]

- Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape
- Only one subject had CTL against all three epitopes
- Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area
- In the review [Menendez-Arias (1998)] the authors note that substitution of three residues in this epitope can confer resistance to RT inhibitors (1, 3, and 6) – substitutions V1E and M6V abolish CTL activity, and M6V confers resistance to 3TC – substitution Y3C reduces CTL activity and is associated with resistance to non-nucleoside RT inhibitors

---

RT(179–187)	RT( )	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Altfeld (2001d)]

- Epitope name: RT VL9. HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested
- Three additional previously described HLA-A2 epitopes were added to the set of 20, including RT VL9, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acutely infected individuals recognized at least 1 (median of 1 and maximum of 2)
- RT VL9 was not recognized by any of the 22 HLA-A2 patients with chronic HIV-1 infection or the 13 HLA-A2 patients with acute HIV-1 infection included in this study

---

RT(179–187)	RT(346–354)	VIYQYMDDL	HIV-1 infection	human(A*0201)	[Dela Cruz (2000)]

- Epitope name: VL9. Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL
- These antigens could also be used to stimulate primary responses *in vitro*

RT(179–187)	RT( )	VIYQYMMDL	HIV-1 exposed seronegative	human(A2)	[Rowland-Jones (1998a)]

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating
- The A and D consensus sequences are both VIYQYMMDL

RT(179–187) Pol(346–354) VIYQYMDDL Vaccine human(A2) [Woodberry (1999)]

Vaccine: *Vector/type:* DNA prime with vaccinia boost *HIV component:* polyepitope

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested
- VIYQYMDDL was recognized by 3 of the HLA-A2 patients

RT(179–187) RT(179–187) VIYQYMDDL HIV-1 infection human(A2) [Schmitt (2000)]

- The mutation M184V confers resistance to lamivudine, and is in the middle of the HLA-A2 epitope VIYQYMDDL
- 1/28 individuals tested produced HIV-1 RT-specific CTL that recognized the peptide representing the lamivudine escape mutants VIYQYVDDL and VIYQYIDDL, but failed to recognize the wildtype epitope VIYQYMDDL
- This suggests immunotherapy stimulating anti-VIYQYVDDL responses may be helpful for reducing lamivudine escape

---

RT(179–187) RT(179–187) VIYQYMDDL HIV-1 infection human(A2) [Haas (1998)]

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)

RT(179–187) Pol(339–347 93TH253 CRF01) VIYQYMDDL HIV-1 infection human(A2) [Sriwanthana (2001)]

- Epitope name: P334-342. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2

RT(179–187) Pol(339–347 93TH253 CRF01) VIYQYMDDL HIV-1 infection human(A2) [Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested
- 2/4 tested FSWs recognized the E clade version of this epitope, which is identical to the previously defined B clade version VIYQYMDDL

	• This epitope was conserved in many subtypes, and exact matches were very uncommon				
RT(179–187)	RT(179–187)	VIYQYMDDL	HIV-1 infection	human(A2)	[Day (2001)]
	• The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP) • Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person				
RT(179–187)	Pol( )	VIYQYMMDL	HIV-1 exposed seronegative	human(A2, A*0202)	[Rowland-Jones (1998b)]
	• HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection • Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world • Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes • This epitope is conserved among A, B and D clade viruses				
RT(180–189)	RT( )	IYQYMDDLYV	HIV-1 infection	human(A*0201)	[Menendez-Arias (1998), van der Burg (1997)]
	• Recognized by CTL from a progressor, spans important RT functional domain • A previous study determined that this was an epitope recognized by a long-term survivor				
RT(181–189)	RT(181–189 LAI)	YQYMDDLYV	HIV-1 infection	human(A*0201)	[Samri (2000)]
	• This epitope contains the mutation M184V, a frequent mutation induced by nucleoside reverse transcriptase inhibitors • High levels of recognition by ELISPOT were observed for zidovudine induced mutation YQYVDDLYV and for the wildtype peptide YQYMDDLYV in patient 250#0 (HLA-A*0201), but neither were recognized by patient 201#5 (also HLA-A*0201) • Both the wild-type and the mutated peptide were computer predicted to have a high binding affinity for A2 (http//bimas.dcrt.nih.gov/molbio/hla_bind)				
RT(192–201)	RT(192–201)	DLEIGQHRTK	HIV-1 infection	human(A3)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules				
RT(192–216)	RT(359–383 HXB2)	DLEIGQHRTKIEELRQ-HLLRWGLTT	HIV-1 infection	human(Bw60)	[Menendez-Arias (1998), Walker (1989)]
	• One of five epitopes defined for RT-specific CTL clones in this study				
RT(192–216)	RT(191–215)	DLEIGQHRTKIEELRQ-HLLRWGFTT	HIV-1 infection	human(polyclonal)	[Haas (1997), Menendez-Arias (1998)]
	• Polyclonal CTL recognition switched from RT 191-215 to RT 514-524 when AZT therapy selected for the resistance mutation, and presumably the escape variant, RT T215Y				

RT(198–212)	RT( )	HRTKIEELRQHLLRW	HIV-1 infection	human( )	[Altfeld (2000)]

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes, and was one of the epitopes presented by a molecule other than B60 in an HLA-B60 individual
- The response to the peptide was CD8 dependent, but the HLA presenting molecule and optimal epitope were not determined

---

RT(201–209)	RT(201–209)	KIEELRQHL	HIV-1 infection	human(A2)	[Haas (1998)]

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules

---

RT(201–210)	Pol( )	KIEELRQHLL		human(B58)	[De Groot (2001)]

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes could stimulate IFNγ production in an ELISPOT assay
- KIEELRQHLL was newly identified as a HLA-B58 epitope in this study, it had been previously shown to be presented by HLA-A2 and Bw60
- KIEELRQHLL did not bind detectably to B7

RT(202–209)	RT( )	IEELRQHLL	HIV-1 infection	human(B60)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B60+ individuals that had a CTL response to this epitope broken down by group: 0/2 group 1, 1/1 group 2, and 0/0 group 3

RT(202–210)	RT(202–210 LAI)	IEELRQHLL		human(B*4001)	[Altfeld (2000), Brander & Goulder(2001)]

- C. Brander notes this is a B*4001 epitope

RT(202–210)	RT( )	IEELRQHLL	HIV-1 infection	human(B60(B*4001)	[Altfeld (2000)]

- This epitope was mapped by ELISPOT in a study identifying new HLA-B60 epitopes
- B60 is present in 10-20% of the Caucasoid and very common in Asian populations

---

RT(202–210)	RT(202–210)	IEELRQHLL	HIV-1 infection	human(B60/B61)	[Day (2001)]

- No immunodominant responses were detected to five B61-restricted epitopes tested
- All five B60-restricted epitopes were reactive in another subject, and the B60-restricted responses together contributed over one-third of the total CTL response

---

RT(203–212)	RT( )	EELRQHLLRW	HIV-1 infection	human(B44)	[Menendez-Arias (1998), van der Burg (1997)]

- The only epitope recognized by CTL from a long-term survivor in two samples taken six years apart
- Recognized by CTL from a progressor, EILKEPVGHGV and TWETWWTEYW were also recognized

RT(209–220)	RT(209–220)	LLRWGLTTPDKK	HIV-1 infection	human(A2)	[Haas (1998)]

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules

RT(243–252)	RT( )	PIVLPEKDSW	HIV-1 infection	human(B*5701)	[Menendez-Arias (1998), van der Burg (1997)]

- Recognized by CTL from a progressor and a long-term survivor, KITTESIVIW was also recognized

RT(243–252)	RT( )	PIVLPEKDSW	HIV-1 infection	human(B*5701)	[Menendez-Arias (1998), van der Burg (1997)]

- Recognized by CTL from a long-term survivor whose CTL response persisted for more than 10 years – the substitution V3M reduced affinity but was well recognized; on the other hand V3T and D8G did not reduce affinity, but abrogated CTL response

RT(243–252)	RT(410–419)	PIVLPEKDSW	HIV-1 infection	human(B57)	[Oxenius (2000)]

- Epitope name: PIV. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable
- None of the 8 study subjects recognized this epitope but none were HLA B57+

RT(244–252)	RT(399–407)	IVLPEKDSW		human(B*5701)	[Brander & Goulder(2001)]

- Subtype of B57 not determined
- C. Brander notes this is a B*5701 epitope

RT(244–252)	RT(244–252 LAI)	IVLPEKDSW	HIV-1 infection	human(B*5701, B*5801)	[Klein (1998)]

- This peptide was defined as the optimal epitope
- B57 has been associated with long-term non-progression in the Amsterdam cohort.
- The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag
- B57 restricted CTL responses are targeted at multiple proteins, but one LTS had a response that was dominated by reactivity to the epitope – two variants were found in this LTS: ITLPEKESW, which bound to B*5701 with similar affinity as the index peptide but was an escape mutant that was not recognized by CTL, and IMLPEKDSW, which bound to B*5701 with reduced affinity but could still be recognized

- In an additional HIV+ LTS, only the variant IELPEKDSW was found, and this epitope was recognized by CTL but had less affinity for B*5701 than the index peptide
- This epitope was recognized in the context of both HLA-B*5701 and B*5801

RT(244–252)	Pol(244–252)	IVLPEKDSW	HIV-1 infection	human(B*5801)	[Appay (2000)]

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T-cells specific for HIV and CMV
- HIV-specific CD8+ T-cells expressed lower levels of perforin than CMV-specific CD8+ T-cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T-cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

RT(244–252)	RT(399–407)	IVLPEKDSW		human(B57)	[van der Burg (1997)]
RT(245–252)	Pol( )	IVPEKDSW	HIV-1 infection	human(B57)	[Kostense (2001)]

- HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load
- Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional
- In 15 of the patients, the proportion of IFNγ producing tetramer cells correlated with AIDS-free survival

RT(260–271)	RT(415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human(B*1501)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*1501 epitope

RT(260–271)	RT(260–271)	LVGKLNWASQIY	HIV-1 infection	human(B62)	[Day (2001)]

- No immunodominant responses were detected to four B62-restricted epitopes tested

RT(260–271)	RT(415–426 IIIB)	LVGKLNWASQIY	HIV-1 infection	human(Bw62)	[Brander & Walker(1996), Menendez-Arias (1998)]

- P. Johnson, Pers. Comm.

RT(263–271)	RT(263–271 LAI)	KLNWASQIY		human(A*3002)	[Brander & Goulder(2001), Goulder (2001b)]

- C. Brander notes this is an A*3002 epitope

RT(263–271)	RT( )	KLNWASQIY	HIV-1 infection	human(A*3002)	[Goulder (2001a)]

- Epitope name: KY9 (RT-35). HLA-A*3002 is very common in African populations, 50% of Zimbabweans express HLA-A30, 44% in African Zulu, so five new HIV epitopes were characterized that are presented by this HLA molecule
- A rapid method was developed combining ELISPOT with intracellular IFN-γ staining of PBMCs to map optimal epitopes, then HLA presenting molecules were defined – this method was completed within 48 to 72 hours of receipt of blood

- Two individuals were studied: Subject 199 (HLA A*0201/*3002 B*4402/51 Cw2/5), a Caucasian, and Subject 6007 (HLA A*3002/ B53/*5801 Cw4/7) an African-Caribbean
- In both HLA-A*3002 individuals the response to RSLYNTVATLY was dominant
- In subject 199 four additional A*3002 epitopes were identified
- Three quantitative assays, ELISPOT, precursor frequency and chromium release, confirmed a hierarchy of response: RY11 (p17) > KY9 (gp41) > KY9 (RT-53) > IY9 (gp41)

RT(268–282)	RT( )	SQIYPGIKVRQLCKL	HIV-1 infection	human( )	[Altfeld (2001a)]

- HIV+ individual AC-06 was tested for reactive overlapping peptides spanning all HIV-1 proteins in an ELISPOT and was found to react with 12 peptides from 7 proteins, suggesting that the breadth of CTL responses is underestimated if accessory proteins are not included in the study
- RT peptides SQIYPGIKVRQLCKL and WKGSPAIFQSSMTKI were recognized

---

RT(269–277)	( )	QIYPGIKVR		(A3)	[Altfeld(2000), Brander & Goulder(2001)]

RT(269–277)	RT(269–277)	QIYPGIKVR	HIV-1 infection	human(A3)	[Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person
- All patients recognized at least 1 A3 epitope, up to 8 A3 epitopes, but none was clearly dominant

---

RT(271–279)	( )	YPGIKVRQL	HIV-1 infection	human(B*4201)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*4201 epitope

RT(271–279)	RT(438–446 IIIB)	YPGIKVRQL	HIV-1 infection	human(B42)	[Menendez-Arias (1998), Wilson (1996)]

- YAGIKVRQL and YPGIKVKQL are naturally occurring variants that are both reactive
- YHKIKVRQL is a naturally occurring variant that has not been tested
- Epitope defined in the context of the Pediatric AIDS Foundation ARIEL Project, a mother-infant HIV transmission study

---

RT(271–279)	Pol(438–446 IIIB)	YPGIKVRQL	HIV-1 infection	human(B42)	[Wilson (1999a)]

- This study describes maternal CTL responses in the context of mother-to-infant transmission
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants
- An additional variant that gave a positive CTL response: YPGIKVKQL, YAGIKVRQL
- YHGIKVRQL was an escape mutant

RT(293–301)	Pol(448–456 SF2-24)	IPLTEEAEL	HIV-1 infection	human(B*3501, B*5101)	[Tomiyama (2000b)]

- Epitope name: HIV-B35-SF2-24. This epitope is naturally processed and presented by both HLA-B*3501 and HLA-B*5101 and is cross-recognized by a single CTL clone
- IPLTEEAEL binds approximately four times more effectively HLA-B*3501 than HLA-B*5101

RT(293–301)	RT(448–456 SF2)	IPLTEEAEL	HIV-1 infection	human(B*3501)	[Menendez-Arias (1998), Tomiyama (1997)]

- A CTL clone responsive to this epitope was obtained
- Only 1/7 B35-positive individuals had a CTL response to this epitope
- An E to K substitution at position 5 abrogates specific lysis, but not binding to B*3501
- An I to V substitution at position 1, P to Q at position 2, and E to K at 5, abrogates specific lysis and binding to B*3501
- An I to V substitution at position 1 did not alter reactivity
- Reviewed in [Menendez-Arias (1998)], this epitope lies in the thumb region of RT

RT(293–301)	( )	IPLTEEAEL	HIV-1 infection	human(B35)	[Kawana (1999)]

- HLA B35 is associated with rapid disease progression
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals but this was one of the six that had no B35 associated pattern of mutation

---

RT(293–301)	RT(448–456 SF2)	IPLTEEAEL	HIV-1 infection	human(B35, B51)	[Menendez-Arias (1998), Shiga (1996)]

- Binds HLA-B*3501 and B*5101
- Reviewed in [Menendez-Arias (1998)], this epitope lies in the thumb region of RT

RT(293–301)	Pol(447–455)	IPLTEEAEL	HIV-1 exposed seronegative, HIV-1 infection	human(B51)	[Kaul (2001a)]

- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers

---

RT(294–318)	RT(461–485 HXB2)	PLTEEAELELAENREIL-KEPVHGVY	HIV-1 infection	human(A2)	[Menendez-Arias (1998), Walker (1989)]

- One of five epitopes defined for RT-specific CTL clones in this study

---

RT(308–317)	RT( )	EILKEPVGHV	HIV-1 infection	human(A*0201)	[Menendez-Arias (1998), van der Burg (1997)]

- Recognized by CTL from a long-term survivor, SPIETVPVKL was also recognized
- Recognized by CTL from a progressor, EELRQHLLRW and TWETWWTEYW were also recognized

---

RT(309–317) RT(476–484) ILKEPVHGV HIV-1 infection human(A*02) [Huang (2000)]

- The single cell ELISPOT assay was optimized and highly specific, and found to work well even after the primary cells had been frozen and thawed
- Increases in γ interferon producing cells were observed in response to anti-retroviral therapy using single cell IFN-γ-production ELISPOT

RT(309–317) RT(476–484) ILKEPVHGV HIV-1 infection human(A*02) [Rinaldo (2000)]

- Administration of triple-drug antiretroviral therapy (IDV, 3TC and ZDV) sometimes showed a transient increase and other times failed to increase CTL responses in patients with advanced HIV disease, but there is a stable population of tetramer stained HIV-specific CD8+ CD45RO+ cells that persist after therapy and long periods of virus being below the level of detection

---

RT(309–317) RT( ) ILKEPVHGV HIV-1 infection human(A*02) [Scott-Algara (2001)]

- Epitope name: IV9. This study examined CTL responses in HLA A*02+ children by tetramer staining for HLA-A2 immunodominant epitopes SLYNTVATL and ILKEPVHGV
- 71% of the 28 HIV-1 infected HLA-A*02 positive children recognized both epitopes, with cells from 26 children stained positive by the gag tetramer (SLYNTVATL) and 21 children by the pol tetramer (ILKEPVHGV)
- There were no differences observed in children that had therapy versus those that did not
- Tetramer-binding cells were memory activated CD28-, CD45RO+, CD45RA- HLADR+, CD69-, CD8+ T-cells

---

RT(309–317) ( ) ILKEPVHGV HIV-1 infection human(A*0201) [Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and was appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

RT(309–317) Pol(476–484) ILKEPVHGV HIV-1 infection human(A*0201) [Spiegel (2000)]

- High levels of CD8+ HIV-1 specific and cytomegalovirus specific CTL were detected by HLA-A*0201-peptide tetramers in 3 infected subjects with very low CD4 counts, but CD8 T-cell mediated effector activity was not seen
- Thus HIV-1 specific CD8+ cells may be present but may lack direct effector activity in late disease, suggesting that overcoming antigen unresponsiveness may be a useful therapeutic strategy

---

RT(309–317) Pol(476–484) ILKEPVHGV HIV-1 infection human(A*0201) [Sewell (1999)]

- Proteasome regulation influences epitope processing and could influence immunodominance
- The proteasome is inhibited by lactacystin treatment, and γ IFN induces expression of proteasome subunits, LMP2 and LMP7, which combine with the proteasome to create an immunoproteasome
- IFN-γ induction of the immunoproteasome and lactacystin inhibition increases the presentation of the A*0201 VIYQYMDDL epitope, but decreases the presentation of the A*0201 ILKEPVHGV epitope, which is immunodominant within pol proteins, showing the two epitopes are processed by different pathways
- ILKEPVHGV seems to be processed by the classical proteasome pathway, while VIYQYMDDL appears to be destroyed by this pathway
- This epitope contains the catalytic site (YMDD) of RT, a conserved sequence in HIV-1 which restricts escape mutants

---

RT(309–317) Pol(476–484) ILKEPVHGV HIV-1 infection human(A*0201) [Loing (2000)]

- The ILKEPVHGV was modified by the addition of an N-palmitoyl-lysine residue at the P0, P1 or P10 positions of the parent peptide to create a lipopeptide for direct antigen delivery to the cytoplasm for processing
- The N-terminal modification increased the life span for functional CTL recognition up to 48 hours in comparison to the parent peptide

---

RT(309–317) Pol(510–518) ILKEPVHGV Vaccine human(A*0201) [Larsson (1999)]

Vaccine: *Vector/type:* vaccinia, canarypox *HIV component:* Gag, Pol, Nef, Env

- ELISPOT was used to assay the CD8 T-cell response to the HIV-1 proteins Gag, Pol, Nef or Env expressed in vaccinia or canarypox vectors in 19 HIV+ people
- The highest CTL frequency was directed at Pol epitopes
- In A*0201 individuals, higher numbers of spot-forming T-cells were directed against HIV-1 proteins expressed in vaccinia than to peptides SLYNTVATL and ILKEPVHGV presented by A2

RT(309–317) RT(476–484) ILKEPVHGV HIV-1 infection human(A*0201) [Wilson (1998a)]

- HIV+ individuals were followed longitudinally using MHC tetramers in combination with 14 anti-BV chain MAbs, and clonal expansion of HIV-specific T-cells was followed *in vivo*
- Seven HIV+ people were studied, and all showed expansions of particular TCR BV clones, often several, relative to uninfected controls
- Three patients were followed in detail, TCR VB expansions persisted for 2 to 3 years, with occasional transient increases

---

RT(309–317) RT(476–484) ILKEPVHGV HIV-1 infection human(A*0201) [Betts (2000)]

- Only 4/11 HLA-A2+ HIV+ individuals had CTL that reacted to SLYNTVATL, calling into question whether it is immunodominant
- Ninety-five optimally-defined peptides from this database were used to screen for γ interferon responses to other epitopes
- 2/11 of the A2+ individuals responded to ILKEPVHGV, and neither of these two responded to SLYNTVATL

RT(309–317) Pol( ) ILKEPVHGV HIV-1 infection human(A*0201) [Gray (1999)]

- Administration of highly active antiretroviral therapy (HAART) reduced CD8+ cell frequency, and the CD8+ cells detected by tetramer staining were likely to be memory cells, indicating that persistently replicating viral populations are needed to maintain high frequencies of HIV-1 specific CTL

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Menendez-Arias (1998), Ogg (1998b)]

- HLA-tetrameric complexes were used in a cross-sectional study of 14 untreated HLA A*0201 positive individuals, revealing an inverse relationship between HIV Gag and Pol specific CTL effector cells (CTLe) and viral load
- Inclusion of both the p17 SLYNTVATL and RT ILKEPVHGV epitopes gives a good representation of HLA A*0201-restricted activity
- No correlation was observed between the CTLe and CD4 count or clearance rate of productively infected cells

RT(309–317)	RT( )	ILKEPVHGV	Vaccine	human(A*0201)	[Hanke (1998a), Hanke (1998b)]

Vaccine: *Vector/type:* vaccinia *HIV component:* polyepitope

- This epitope was shown to be processed and presented to appropriate CTL clones upon infection of human target cells with vaccinia virus Ankara (VVA) carrying 20 HIV-1 epitopes recognized by humans

RT(309–317)	RT(476–484)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[Konya (1997), Menendez-Arias (1998)]

- This epitope was included as a positive control
- Binding affinity to A*0201 was measured, $C\_1/2\text{max}\mu M = 12$

RT(309–317)	RT(468–476)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[van der Burg (1996)]

- Immunogenic in humans, slow dissociation rate, and associated with immunogenicity in transgenic HLA-A*0201/K^b mice
- CTL generated by *in vitro* stimulation of PBMC derived from uninfected individual

RT(309–317)	RT(468–476)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[van der Burg (1995)]

- Binds HLA-A*0201 – CTL generated by *in vitro* stimulation of PBMC from an HIV negative donor

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Menendez-Arias (1998), Pogue (1995)]

- Mutational study: position 1 I to Y increases complex stability with HLA-A*0201

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Goulder (1997e), Goulder (1997a), Menendez-Arias (1998)]

- Identical twin hemophiliac brothers were both infected with the same batch of factor VIII
- One had a response to gag A2 epitope SLYNTVATL, the other to pol A2 epitope ILKEPVHGV
- Viral sequencing from the twin that had no response to SLYNTVATL indicated his virus had the substituted form SLHNAVAVL
- 71% of an additional set of 22 HIV-1 infected HLA-A*0201 positive donors preferentially responded to gag SLYNTVATL
- Those individuals with a pol ILKEPVHGV response tended to have mutations in or around SLYNTVATL
- [Goulder (1997a)] is a review of immune escape that summarizes this study

RT(309–317)	RT(309–317)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Altman (1996)]

- This paper introduces the tetramer methodology which permits quantification of specific CTL based on expression of specific TCRs – HLA-A2 tetramers were prepared that can stain CTL lines specific for ILKEPVHGV and SLYNTVATL, and quantify HIV-specific CD8+ cell lines in freshly isolated PBMCs
- Three patients only stained the Gag epitope SLYNTVATL, one patient had the highest frequency of tetramer staining to the Pol epitope (0.77%), less to the Gag epitope (0.28%)
- The A2-Pol CD8+ clones were CD45RO positive and HLA-DR and CD38 negative, suggesting a memory rather than effector phenotype

---

RT(309–317)	RT(476–484)	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[Menendez-Arias (1998), Walter (1997)]

- HLA-A2 heavy chain and β2-microglobulin expressed in *E. coli* were refolded in the presence of this peptide
- The HLA-A2-peptide complex elicited HLA-A2 peptide-specific CTL response in cells lacking HLA-A2
- Suggests that preformed HLA-peptide complexes could provide an alternate to intracellular processing for immunogens

---

RT(309–317)	RT(464–472)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Gray (1999)]

- Peptide-tetramer complexes of A*0201 and SLYNTVATL or ILKEPVHGV were used to study individuals receiving HAART to determine the frequency of Class I HLA-restricted anti-HIV CD8+ T-cells
- 17/18 asymptomatic patients had a CTL response to one or both epitopes – 72% had a CTL response to SLYNTVATL
- After HAART, the majority of the epitope-specific CTL were apparently memory cells

---

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Brander (1998), Brander & Goulder(2001)]

- Of 17 infected HLA A*0201 subjects, 13 had CTL responses against the p17 SLYNTVATL epitope, six recognized ILKEPVHGV and five recognized VIYQYMDDL, and there was no correlation between viral load and recognition of a specific epitope or evidence of immune escape
- Only one subject had CTL against all three epitopes
- Subjects were part of the San Francisco City Clinic Cohort, the ARIEL project and from the Boston area
- C. Brander notes this is an A*0201 epitope

RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Ogg (1999)]

- CTL effector levels were measured after potent ARV therapy using HLA-tetramer complexes for the A*0201 epitopes SYLVANTVATL and ILKEPVHGV in seven patients, and the B*3501 epitope DPNPQEVVL in one additional patient
- Levels of CTL effectors typically decline for 5-7 days and then rebound, fluctuating during the first two weeks of therapy
- After the early fluctuation, there was a steady exponential decay with a median half-life of 45 days

---

RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Brander & Goulder(2001)]

- C. Brander notes this is an A*0201 epitope

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection, *in vitro* stimulation	human(A*0201)	[Dela Cruz (2000)]

- Epitope name: IV9. Integration of HIV RT CTL epitopes into the N-terminus of the HLA-A2 heavy chain, or tethering the epitopes to the target chain, resulted in epitope-specific lysis by CD8+ CTL
- These antigens could also be used to stimulate primary responses *in vitro*

RT(309–317)	RT(309–317)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Samri (2000)]

- Epitope name: P1. The epitope was recognized by patient 250#0 but not in another A*0201+ patient, 201#5, in a study of the effects of therapy escape mutations on CTL recognition

---

RT(309–317)	Pol( )	ILKEPVHGV	*in vitro* stimulation	human(A*0201)	[Engelmayer (2001)]

- Recombinant canarypox virus vector containing HIV-1 sequences, upon infection of mature dendritic cells, can trigger specific lysis through *in vitro* by T-cells from HIV-1 infected individuals at levels comparable to the response seen to HIV carried in vaccinia vectors
- Recombinant canarypox virus vector containing HIV-1 sequences can also stimulate HIV-specific CD4+ helper T-cell responses

---

RT(309–317)	Pol( )	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Gea-Banacloche (2000)]

- In a study including many long-term non-progressors, no correlation between plasma virus levels and number of HIV-specific CD8+ T-cells was found
- High frequencies of circulating CD8+ T-cells were HIV-1 specific, and the majority of these responses were to gag-pol gene products
- 4/21 subjects were HLA-(A*0201), and of these only 2 subjects (patients 3 and 19) tested positive to this epitope

---

RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Jin (2000a)]

- The CTL effector levels (CTLe) were compared in long term non-progressors (LTNP) with low viral load and in patients whose virus was well-suppressed by therapy, using a tetramer assay
- LTNPs have high memory CTLe numbers and low viral load, while HAART patients had low CTLe numbers and low viral load

---

RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Appay (2000)]

- Combined tetramer and intracellular cytokine staining was used to study the function of circulating CD8+ T-cells specific for HIV and CMV
- HIV-specific CD8+ T-cells expressed lower levels of perforin than CMV-specific CD8+ T-cells from the same donor, and this was associated with persistent CD27 expression on HIV-specific cells, suggesting impaired maturation
- In most donors, between 50% and 95% of the activated virus-specific CD8+ T-cells produced IFN-γ and MIP-1β with a distinct subset that failed to produce TNF-α

RT(309–317)	Pol( )	ILKEPVHGV	HIV-1 infection	human(A*0201)	[Ostrowski (2000)]

- The role of CD4+ T-cell help in expansion of virus-specific memory CTL was studied through co-culture *ex vivo*
- Optimal expansion of HIV-1-specific memory CTL depended on CD4+ T-cell help in 9/10 patients – CD40 ligand trimer (CD40LT) could enhance CTL in the absence of CD4+ T-cell help to a variable degree in most of patients
- Those CTL that didn't respond to CD40LT could expand with IL-2 present, and IL-15 produced by dendritic cells also contributes
- The T-helper epitope used for CD4+ T-cell stimulation was the universal tetanus helper epitope TET830-843 (QYIKANSKFIGITE)

RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	HIV-1 infection	human(A*0201, A*0205)	[Mollet (2000)]

- Epitope name: P1. A panel of 16 epitopes covering 15 class I alleles was tested in 14 HIV+ patients from an unselected Caucasian population treated with HAART, using tetramer staining or CD8+ cell IFNγ production to measure responses
- In general, during the first month of treatment viral load decreased and frequencies of HIV-specific CTL tripled and broadened – eight new HIV specificities that were not previously detectable were newly detected, as were CMV specific CD8+ PBL – but with continued viral suppression, HIV-specific responses diminished
- Viral rebounds gave different patterns of response: increases or decreases in pre-existing response, new specificities, or no change

---

RT(309–317)	Pol(476–484)	ILKEPVHGV	Vaccine	human(A2)	[Woodberry (1999)]

Vaccine: *Vector/type:* vaccinia *HIV component:* polyepitope

- A polyepitope vaccine was generated in a vaccinia construct that contiguously encoded seven epitopes, all presented by HLA A-2
- HHD mice have a transgene of HLA A2 linked to the transmembrane and cytotoxic domains of H-2D^d – this transgene is the only MHC molecule expressed in the mice
- CTL responses to Gag (77-85) SLYNTVATL, Pol (476-484) ILKEPVHGV, gp120 (120-128) KLTPLCVTL, and Nef (190-198) AFHHVAREL were observed in HIV polytope HHD-vaccinated mice, and these responses were enhanced with vaccinia boost
- No CTL immune responses were generated against HLA A2-restricted HIV epitopes Nef 157-166 (PLTFGWCYKL), Pol 346-354 (VIYQYMDDL), and Nef 180-189 (VLEWRFDSRL)
- Sixteen HLA A2+ patients were tested for their ability to make CTL responses by peptide restimulation in culture with the epitopes selected for inclusion in the polytope – one individual recognized all seven of these epitopes; 7 patients had CTL cultures able to recognize at least one of the epitopes, and 6 of those 7 recognized more than one epitope, but they were not able to test all peptides for all patients; many patients only had three peptides tested
- ILKEPVHGV was recognized by 2 of the patients

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Kolowos (1999)]

- TCR usage in CTL specific for this epitope was examined in three patients and identical Vβ6.1 and Vα2.5 gene segments were used and two of the patients had very similar complementarity-determining regions – clonal expansion of RT-HIV-specific CTL can contribute to the skewed TCR repertoire in HIV-1 infected patients
- CTL clones from all three patients showed similar sensitivity to mutation in the epitope, `-------E-` was well recognized (the sequence from SF2), `---D-----` was not (the common A clade form)

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Collins (1998)]

- Nef down-regulates MHC class I molecules, which inhibits CTL killing of HIV-infected targets
- The anti-RT CTL clone killed Nef- cells less efficiently than anti-gag clones, correlated with the reduced expression of RT

RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	HIV-1 infection	human(A2)	[Fan (1997)]

- The capacity of dendritic cells to process and present antigen and stimulate anti-HIV-1 CTL memory responses was studied

---

RT(309–317)	RT(464–472)	ILKEPVHGV	HIV-1 infection	human(A2)	[Kundu (1998b)]

- Allogeneic dendritic cells (DCs) were obtained from HLA-identical siblings, pulsed with rgp160 MN or A2-restricted HIV-1 epitope peptides, and infused monthly into six HIV-infected patients
- 1/6 showed increased env-specific CTL and increased lymphoproliferative responses, 2/6 showed increase only in proliferative responses, and 3/6 showed no change – pulsed DCs were well tolerated
- ILKEPVHGV is a conserved HLA-A2 epitope included in this study – 5/6 patients had this sequence as their HIV direct sequence, and these had a detectable CTL response– one person carried the form ILREPVHGV and had no detectable CTL

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Menendez-Arias (1998), Tsomides (1994)]

- CTL clones recognize naturally processed peptide – peptide abundance corresponded to level of CTL killing

---

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 exposed seronegative	human(A2)	[Rowland-Jones (1998a)]

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating
- The A subtype consensus is ILKDPVHGV
- The D subtype consensus is identical to the epitope ILKEPVHGV

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Cao (1997), Menendez-Arias (1998)]

- The consensus peptides of B and D clade viruses and some As have the sequence ILKEPVHGV
- The consensus peptide of a subset of A clade viruses, ILKDPVHGV, is not cross-reactive

---

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Menendez-Arias (1998), Yang (1996)]

- CD4+ cell lines acutely infected with HIV were studied to determine their susceptibility to lysis by CTL
- Clones specific for RT lysed HIV-1 infected cells at lower levels than Env or Gag specific clones
- The distinction was thought to be due to lower expression of RT relative to Env and Gag
- CTL can lyse infected cells early after infection, possibly prior to viral production

---

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Yang (1997a)]

- CTL inhibit HIV-1 replication at effector cell concentrations comparable to those found *in vivo*
- CTL produced HIV-1-suppressive soluble factors – MIP-1α, MIP-1β, RANTES, after antigen-specific activation
- CTL suppress HIV replication more efficiently in HLA-matched cells

---

RT(309–317)	RT(309–317)	ILKEPVHGV	HIV-1 infection	human(A2)	[Menendez-Arias (1998), Moss (1995)]

- Two clones were obtained with different TCR usage, V_β1 and V_β21

RT(309–317)	RT(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Menendez-Arias (1998), Musey (1997)]
• Cervical CTL clones from an HIV-infected woman recognized this epitope					
RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	HIV-1 infection	human(A2)	[Menendez-Arias (1998), Tsomides (1991)]
• Precise identification of the nonamer that binds to A2					
RT(309–317)	RT(476–484 LAI)	ILKEPVHGV	Peptide-HLA interaction	human(A2)	[Connan (1994), Menendez-Arias (1998)]
• Promotes assembly of HLA-A2 molecules in T2 cell lysates					
RT(309–317)	RT(510–518)	ILKEPVHGV	*in vitro* stimulation	human(A2)	[Parker (1992)]
• Studied in the context of HLA-A2 peptide binding					
RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A2)	[Dyer (1999)]
• CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load					
RT(309–317)	RT(476–484)	ILKEPVHGV	*in vitro* stimulation	human(A2)	[Zarling (1999)]
• This study compares the ability of macrophages and dendritic cells to stimulate primary responses in CD8+ lymphocytes isolated from HLA-appropriate HIV-uninfected donors using peptide-pulsed APC – the dendritic cells performed better as APC for the stimulation of primary responses • Strong CTL responses were elicited by the epitopes DRFYKTLRA and GEIYKRWII when presented by either immature or mature dendritic cells – macrophages were not able to prime a CTL response against DRFYKTLRA • A weak response to KLTPLCVSL was stimulated using macrophages as the APC • No detectable response was observed for the following previously-defined HIV epitopes: KIRLRPGGK, ILKEPVHGV, IRLRPGGK, GPKVKQWPL					
RT(309–317)	RT( )	ILKEPVHGV	computer prediction	(A2)	[Schafer (1998)]
• This study uses EpiMatrix for T-cell epitope prediction to identify possible HLA-B27 and A-2 CTL epitopes in HIV • Based on EpiMatrix predictions, 28 peptides were synthesized and tested using T2 binding assays for potential HLA A2 or B27 binding, and 12 of these were shown to bind to the predicted HLA molecule • Two of these 12 peptides had been previously identified as CTL epitopes: HLA-B27 KRWILGLNK and HLA-A2 ILKEPVHGV • This sequence is not conserved between clades, but is found only in a small number of B clade isolates					
RT(309–317)	RT( )	ILKEPVHGV	HIV-1 infection	human(A2)	[Altfeld (2001d)]
• Epitope name: RT IV9. HIV was scanned for all peptides which carried the A2-supermotif pattern conserved in more than 50% of B clade sequences – 233 peptides met this criteria, and 30 of these bound to HLA-A*0201 – 20/30 bound to at least 3/5 of HLA-A2 supertype alleles tested					

- Three additional previously described HLA-A2 epitopes were added to the set of 20, and 18/22 chronically infected HLA-A2 individuals had CTL that recognized at least one of the 23 peptides (median of 2 and maximum of 6), while 6/12 acutely infected individuals recognized at least 1 (median of 1 and maximum of 2)
- This peptide binds to four HLA-A2 supertype alleles: A*0201, A*0202, A*0206 (highest affinity) and A*6802
- RT IV9 was recognized in 7/22 patients with chronic HIV-1 infection
- 1/13 patients with acute HIV-1 infection recognized RT IV9

RT(309–317) Pol( ) ILKDPVHGV HIV-1 infection human(A2) [Kaul (2001b)]

- This study examines CTL responses in HIV-exposed, persistently seronegative individuals, HEPS, who eventually seroconverted – 11/114 HEPS Nairobi sex workers eventually seroconverted, and for six of these HIV CTL reactive epitopes had been defined while seronegative
- ILKDPVHGV or ILKEPVHGV was recognized in 1 of the 6 women (ML1760), and the response was present in the last available sample prior to seroconversion, 12 months
- 20/20 sequences of the infecting strain had no substitutions in this epitope, all were ILKDPVHGV, so there was no evidence for escape
- The epidemiological factor associated with seroconversion was stopping sex work and HIV-specific CTL activity declines when HEPS sex workers stop working for a period or retire
- This epitope was recognized by 4/22 HEPS control sex workers: ML887, ML1192, ML1250, and ML1749

RT(309–317) RT(476–484) ILKEPVHGV HIV-1 infection human(A2) [Oxenius (2000)]

- Epitope name: ILK. Patients who started therapy at acute HIV-1 infection (three with sustained therapy, two with limited therapy upon early infection) had strong HIV-specific CD4 proliferative responses and were able to maintain a CTL response even with undetectable viral load – three patients that had delayed initiation of HAART had no HIV-specific CD4 proliferative responses and lost their CTL responses when HAART was eventually given and their viral loads became undetectable
- One of the 2/8 HLA-A2+ study subjects recognized this CTL epitope
- Patient SC9 (HLA A1/2, B8/13, Cw0/0701, DR2/11, DQ6/7) had a CTL response against epitopes FLKEKGGL, ILKEPVHGV, SQRRQDILDLWIYHTQGYFPDWQNY, and GEIYKRWII and all responses declined during therapy initiated at day 390 but were restored when therapy became intermittent

---

RT(309–317) Pol( ) ILKEPVHGV HIV-1 infection human(A2) [Kostense (2001)]

- HLA tetramers to six epitopes were used to study HLA-A2, B8 and B57 CTL in 54 patients – HIV-specific tetramer positive cells were inversely correlated with viral load in patients with high CD4, but in patients with CD4 T-cells below 400 high tetramer frequencies were found despite high viral load
- Most patients have high levels of HIV-specific T-cell expansions, but many of these cells aren't functional
- In 15 of the patients, the proportion of IFNγ producing tetramer cells correlated with AIDS-free survival

---

RT(309–317) Pol( ) ILKEPVHGV HIV-1 infection human(A2) [Seth (2001)]

- CTL responses were studied by tetramer staining in 41 patients with combination therapy – activated CD8+ T-cells decline as the viral load drops in response to therapy, but the overall level of antigen-specific cells capable of differentiating into effectors stays constant and new epitopes may be recognized

- 6/10 A*0201+ individuals had HIV-specific tetramer staining cells, and 5 of these 6 declined upon successful therapy
- 3/10 A*0201+ individuals with chronic HIV-1 infection recognized this epitope
- Prior to therapy, the mean percentage of CD8+ cells that recognized the immunodominant epitope SLYNVATL was six-fold greater than the percentage recognizing the epitope ILKEPVHGV

RT(309–317) RT(476–484 SF2) ILKEPVHGV HIV-1 infection human(A2) [Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-A2+ individuals that had a CTL response to this epitope broken down by group: 1/10 group 1, 0/6 group 2, and 3/4 group 3

RT(309–317) Pol(476–484) ILKDPVHGV HIV-1 exposed seronegative, HIV-1 infection human(A2) [Kaul (2001a)]

- Variants ILK(D/E)PVHGV are A/B clade specific
- ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers
- Responses in HEPS women tended to be lower, and focused on different epitopes with HLA presenting molecules that have previously been associated with reduced risk of infection, and there was a shift in the response in the HEPS women upon late seroconversion to epitopes recognized by the HIV-1-infected women
- 43/91 HEPS women had CD8+ responses and detection of HIV-1-specific CTL in HEPS women increased with the duration of viral exposure
- Among HLA-A2 women, 7/10 HEPS and 14/26 HIV-1-infected women recognized this epitope, and ILK(D/E)PVHGV tended to be more reactive in HEPS women, SL(F/Y)NTVATL in infected women
- The dominant response to this HLA allele was to this epitope in all 7/10 HEPS cases but in only 5 of the 14/26 HIV-1-infected women
- Four epitopes were considered to be “resistant epitopes”, as they were preferentially reactive in HEPS women and so may confer resistance, and these were found in three different proteins: A2 ILKD/EPVHGV in RT, A*6802 DTVLEDINL in Protease, B14 DLNM/TLNI/VV in p24 and B18 FRDYVDRFY/FK also in p24
- Differences in epitope specificity were only seen for responses restricted by class I HLA alleles A2, A24, A*6802, B14, and B18, previously shown to be associated with resistance to HIV-1 in this cohort
- Subject ML 1250 had an A2 response to ILKD/EPVHGV prior to seroconversion, which switched to SLF/YNTVATL post-seroconversion
- Subject ML 1760 had an A2 response to ILKD/EPVHGV prior to seroconversion, and gained responses to epitopes A2 SLF/YNTVATL and B27 KRWIIL/MGLNK post-seroconversion

---

RT(309–317)	Pol( )	ILRIPVHGV	HIV-1 infection	human(A2)	[Sriwanthana (2001)]

- Epitope name: P464-472. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was reactive in HIV+ control study subject 144 who carried HLA-A2

RT(309–317)	Pol( )	ILRIPVHGV	HIV-1 infection	human(A2)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive so the study concentrated on A11 epitopes, although E clade versions of previously defined B-clade A2 and A24 epitopes were also tested
- 1/4 tested FSWs recognized the E clade version of this epitope, which differs from the previously defined B clade version by two amino acids: ILKEPVHGV
- This epitope was not conserved in many subtypes, and exact matches were very rare

---

RT(309–317)	RT(309–317)	ILKEPVHGV	HIV-1 infection	human(A2)	[Day (2001)]

- The CTL response to optimally defined CTL epitopes restricted by HLA class I A and B alleles in individuals who co-expressed HLA A2, A3, and B7 was studied in eight HIV-1-infected subjects, two with acute infection, five with chronic, and one long-term non-progressor (LTNP)
- Two to 17 epitopes were recognized in a given individual, A2-restricted CTL response tended to be narrow and never dominated the response, and 25/27 epitopes were targeted by at least one person

---

RT(309–317)	Pol(476–484)	ILKEPVHGV	HIV-1 infection	human(A2 supertype)	[Propato (2001)]

- Long-term nonprogressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term nonprogressors recognized far fewer epitopes
- Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs
- A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus
- This epitope can bind three of the five HLA-A2 supertypes alleles (A*0201, A*020 2, A*0203, A*0206 and A*6802)

RT(309–317)	Pol(464–472)	ILKEPVHGV	HIV-1 infection	human(A2, A*0201)	[Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

---

RT(309–317)	Pol( )	ILKEPVHGV	HIV-1 exposed seronegative	human(A2, A*0202)	[Rowland-Jones (1998b)]

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes
- This epitope is conserved among B and D clade viruses

- Clade A version of the epitope, ILKDPVHGV, was preferentially recognized by CTL

RT(309–317)	RT(309–317)	ILKEPVHGV	Vaccine, *in vitro* stimulation	human, murine(A2, A2 transgenic)	[De Berardinis (2000)]

Vaccine: *Vector/type:* HIV-1 peptide in filamentous bacteriophage major coat protein *HIV component:* RT peptides

- Epitope name: RT2. Phage display of the CTL epitope, ILKEPVHGV coupled with T helper epitope KDSWTVNDIQKLVGK, elicited specific CTL responses *in vitro* in PBMC from HIV negative individuals and *in vivo* upon immunization of HLA-A2 transgenic mice
- Bacteriophage presentation of peptides is generally used for stimulation of antibodies, and this novel discovery of CTL epitope processing and presentation suggests new possibilities for these vectors

RT(309–317)	Pol( )	ILKEPVHGV	Vaccine	SJL/J HLA transgenic mice(A2.1)	[Ishioka (1999)]

Vaccine: *Vector/type:* DNA *HIV component:* polyepitope

- A minigene vaccine construct encoding 6 HLA 2.1 and 3 HLA A11 restricted CTL epitopes, the universal Th cell epitope PADRE (pan-DR epitope) and an ER translocating signal sequence was constructed
- The epitopes were chosen for dominant recognition by CTLs during HBV and HIV infections in humans
- HLA transgenic mice were used for quantitating *in vivo* immunogenicity of DNA vaccines encoding HLA-restricted CTL epitopes – strong responses were observed to all nine epitopes, and CTL memory persisted up to four months after a single injection

RT(309–318)	RT(476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human(B*1501)	[Brander & Goulder(2001)]

- C. Brander notes this is a B*1501 epitope

RT(309–318)	RT(309–318)	IKLEPVHGVY	HIV-1 infection	human(B62)	[Day (2001)]

- No immunodominant responses were detected to four B62-restricted epitopes tested

RT(309–318)	RT(476–485 LAI)	ILKEPVHGVY	HIV-1 infection	human(Bw62)	[McMichael & Walker(1994), Menendez-Arias (1998)]

- Review of HIV CTL epitopes

RT(328–336)	RT(175–183 SF2)	NPDIVIYQY	HIV-1 infection	human(B35)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B35+ individuals that had a CTL response to this epitope broken down by group: 1/2 group 1, 0/2 group 2, and 1/1 group 3

RT(328–352)	RT(495–515 LAI)	EIQKQGQGQWTYQIY-QEPFKNLKTG	HIV-1 infection	human(A11)	[Menendez-Arias (1998), Walker (1989)]
• One of five epitopes defined for RT-specific CTL clones in this study					
RT(340–350)	RT(507–516)	QIYQEPFKNLK	HIV-1 infection	human( )	[Menendez-Arias (1998), Price (1995)]
• Study of cytokines released by HIV-1 specific activated CTL					
RT(340–350)	Pol(487–497 93TH253 CRF01)	QIYQEPFKNLK	HIV-1 exposed seronegative, HIV-1 infection	human(A11)	[Sriwanthana (2001)]
• Epitope name: P495-505. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand • HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed • This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33 • This epitope was reactive in HIV+ study subjects 053 and 184 who carried HLA-A11					
RT(340–350)	Pol(487–497 93TH253 CRF01)	QIYQEPFKNLK	HIV-1 infection	human(A11)	[Bond (2001)]
• HLA-A11 CRF01 (called subtype E in Bond *et al*.) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive • Seventy-seven possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified • This epitope was not predicted by the EpiMatrix method to be likely to bind to A11, though it served as an epitope in the FSWs, and it was one of the six A11 epitopes that had been previously defined • 5/8 tested FSWs recognized this epitope • This epitope was highly conserved in other subtypes, although exact matches were not very common					
RT(340–352)	RT(507–519 LAI)	QIYQEPFKNLKTG	HIV-1 infection	human(A11)	[Johnson & Walker(1994), Menendez-Arias (1998)]
• This epitope was listed in a review					
RT(340–352)	Pol(495–507)	QIYQEPFKNLKTG	HIV-1 infection	human(A11)	[Ferrari (2000)]
• One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles					
RT(341–350)	RT(508–516)	IYQEPFKNLK	HIV-1 infection	human(A*1101)	[Culmann(1998)]
• C. Brander notes that this is an A*1101 epitope in the 1999 database					

RT(341–350)	RT(508–517 LAI)	IYQEPFKNLK	HIV-1 infection	human(A*1101)	[Brander & Goulder(2001)]
• C. Brander notes this is an A*1101 epitope					
RT(341–350)	RT(508–517 SF2)	IYQEPFKNLK	HIV-1 infection	human(A11)	[Altfeld (2001c)]
• Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection • The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef • Previously described and newly-defined optimal epitopes were tested for CTL response • Number of HLA-A11+ individuals that had a CTL response to this epitope broken down by group: 0/3 group 1, 0/0 group 2, and 1/2 group 3					
RT(341–350)	Pol(508–516)	IYQEPFKNLK	HIV-1 exposed seronegative, HIV-1 infection	human(A11)	[Kaul (2001a)]
• ELISPOT was used to study CTL responses to a panel of 54 predefined HIV-1 epitopes in 91 HIV-1-exposed, persistently seronegative (HEPS) and 87 HIV-1-infected female Nairobi sex workers					
RT(356–365)	Pol(511–520 HXB2)	RMRGAHTNDV	HIV-1 infection	human(A*3002)	[Mulligan (2001)]
• Epitope P52 from Patient 11113 with HLA genotypes A*2904, A*3002, B*1503, B*5802, Cw*0202, Cw*0602					
RT(364–372)	RT(518–526 U455)	DVKQLTEVV		human(A28, A*6802)	[Dong(1998), Menendez-Arias (1998)]
• Predicted on binding motif, no truncations analyzed • Reacts with clade A consensus (U455), and with the peptide DVKQLAEAV, from the D clade					
RT(364–372)	RT(470–478 clade A)	DVKQLTEVV	HIV-1 infection	human(B70)	[Dorrell (1999)]
• CTL responses in three individuals with non-clade B infections were studied, two with subtype A infections, one with subtype C – their infections all originated in East Africa • This CTL response was defined in a patient with an A subtype infection • Bulk cultures from this patient gave a CTL response that could recognize the subtype D form of this epitope, with two substitutions (DVKQLAEAV), though a CTL line from these cultures didn't recognize the B clade variant (DVKQLTEAV)					
RT(374–383)	RT( )	KITTESIVIW	HIV-1 infection	human(B*5701)	[Menendez-Arias (1998), van der Burg (1997)]
• Patients studied were from the Amsterdam cohort • CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS); no differences could be found in the degree of conservation in the two groups • Epitope recognized by LTS and by a progressor					

RT(374–383)	RT( )	KITTESIVIW	HIV-1 infection	human(B*5701)	[van der Burg (1997)]

- Recognized by CTL from a progressor and a long-term survivor, PIVLPEKDSW was also recognized

RT(375–383)	RT(375–383 LAI)	ITTESIVIW	HIV-1 infection	human(B*5701 B*5801)	[Klein (1998)]

- Another patient recognized the ten-mer version of this epitope, KITTESIVIW [van der Burg (1997)]
- B57 has been associated with long-term non-progression in the Amsterdam cohort
- The most pronounced CTL responses in HLA B*5701 LTS were to RT and Gag
- The patient that recognized ITTESIVIW also recognized IVLPEKDSW

RT(375–383)	RT(375–383 SF2)	ITTESIVIW	HIV-1 infection	human(B57)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response
- Number of HLA-B57+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 0/0 group 2, and 1/2 group 3

RT(392–401)	RT(559–568 LAI)	PIQKETWETW		human(A*3201)	[Harrer (1996b), Menendez-Arias (1998)]

- Reviewed in [Menendez-Arias (1998)], suggest the epitope is HLA B53/Cw2
- C. Brander notes that this is an A*3201 epitope in the 1999 database

RT(392–401)	RT(559–568 LAI)	PIQKETWETW		human(A*3201)	[Brander & Goulder(2001)]

- C. Brander notes this is an A*3201 epitope

RT(392–401)	Pol(547–556 HXB2)	PIQKETWETW	HIV-1 infection	human(A*3201)	[Mulligan (2001)]

- Epitope P55 from Patient 07118 with HLA genotypes A*0209, A*3201, B*4002, B*5301, Cw*0202, Cw*0401
- Epitope P55 Patient 07118 has 4 more optimal peptides N10, KEKGGLEGL with HLA B*4002; G21 and G22, AEWDRVHPV with HLA B*4002; G31, QASQEVKNW with HLA B*5301;G43, TERQANFL with HLA B*4002

RT(392–401)	RT(559–568 SF2)	PIQKETWETW	HIV-1 infection	human(A32)	[Altfeld (2001c)]

- Therapy provided during acute infection resulted in a narrower CTL response, stronger T help response, and a less diverse viral population than was seen in individuals treated during chronic infection
- The breadth and specificity of the response was determined using ELISPOT by studying 19 individuals with pre-seroconversion therapy (Group 1), 11 individuals with primary infection but post-seroconversion therapy (Group 2), and 10 individuals who responded to HAART given during chronic infection (Group 3), using 259 overlapping peptides spanning p17, p24, RT, gp41, gp120 and Nef
- Previously described and newly-defined optimal epitopes were tested for CTL response

- Number of HLA-A32+ individuals that had a CTL response to this epitope broken down by group: 0/0 group 1, 1/1 group 2, and 0/0 group 3

RT(397–406)	RT( )	TWETWWTEYW	HIV-1 infection	human(B44)	[Menendez-Arias (1998), van der Burg (1997)]

- Recognized by CTL from two progressors
- EILKEPVGHGV and EELRQHLLRW were also recognized by one, and RETKLGKAGY was also recognized by the other

RT(416–424)	Pol(563–571 93TH253 CRF01)	FVNTPPLVK	HIV-1 exposed seronegative	human(A11)	[Sriwanthana (2001)]

- Epitope name: P571-579. This was a study of HIV-1 exposed persistently seronegative (HEPS) female sex workers in Chiang Mai, northern Thailand
- HLA-A11 is very common in this population, and was enriched among the HEPS sex workers – weak CTL responses were detected in 4/7 HEPS women, and CTL responses were found in 8/8 HIV+ controls, and 0/9 HIV- women that were not exposed
- This epitope was weakly reactive in the HEPS study subject 128 who was HLA A11/A33

RT(416–424)	Pol(563–571 93TH253 CRF01)	FVNTPPLVK	HIV-1 infection	human(A11)	[Bond (2001)]

- HLA-A11 CRF01 (called subtype E in Bond *et al.*) epitopes were identified that stimulated CTL from HIV+ female sex workers (FSW) from Northern Thailand, of whom more than half were HLA-A11 positive
- 77 possible HLA-A11 epitopes were first defined using EpiMatrix, these were screened for binding to A11 and 26 bound, and 12 of these were epitopes for CTL responses from 8 HLA-A11 positive FSWs, six were novel, six were previously identified
- This is one of the new A11 epitopes identified through the streamlined EpiMatrix method, and 1/8 tested FSWs recognized it
- This epitope was conserved many subtypes (but not subtype H), but exact matches were not very common

RT(421–429)	RT(421–429)	PLVKLWYQL	HIV-1 infection	human(A2)	[Haas (1998)]

- Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively)
- New clusters of epitopes were defined utilizing different HLA molecules

RT(432–440)	RT(587–597 SF2)	EPIVGAETF	HIV-1 infection	human(B*3501)	[Menendez-Arias (1998), Tomiyama (1997)]

- A CTL clone responsive to this epitope was obtained
- 5/7 B35-positive individuals had a CTL response to this epitope
- An E to D substitution at position 1, and V to I at position 4, reduces activity but not binding to B*3501
- [Menendez-Arias (1998)] note in their review that this epitope is near the protease cleavage site and conservation of this region is important for proper viral maturation

RT(432–440)	Pol(587–595)	EPIVGAETF	HIV-1 infection	human(B*3501)	[Tomiyama (2000a)]

- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A

- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

RT(432–440) ( ) EPIVGAETF HIV-1 infection human(B35) [Wilson (2000)]

- Three individuals with highly focused HIV-specific CTL responses were studied during acute infection using tetramers – high frequencies of HIV-1-specific CD8+ T-cells were found prior to seroconversion, and a close temporal relationship between the number of circulating HIV-specific T-cells and viral load was also found
- All three patients were B*2705, with HLA alleles: A1, A30/31, B*2705, B35; A1, A*0301, B7, B*2705; and A*0201, A*0301, B*2705, B39
- ELISPOT was used to test a panel of CTL epitopes that had been defined earlier and was appropriate for the HLA haplotypes of the study subjects – 3/3 subjects showed a dominant response to the B*2705 epitope KRWIILGGLNK
- The subject with A*0201 had a moderately strong response to SLYNTVATL
- Weak responses were observed to A*301-RLRPGGKKK, A*301-QVPLRPMTYK, and B7-TPGPGVRYPL in the subject who was HLA A1, A*0301, B7, B*2705
- No acute response was detected to the following epitopes: A*201-ILKEPVHGV, A*301-KIRLRPGGK, A*301-AIFQSSMTK, A*301-TVYYGVPVWK, B35-EPIVGAETF, B35-HPDIVIYQY, B35-PPIPVGEIY, B35-NSSKVSQNY, B35-VPLRPMTY, B35-DPNPQEVVL

RT(432–440) Pol(587–595) EPIVGAETF HIV-1 infection human(B35) [Dyer (1999)]

- CTL specific responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load

---

RT(432–440) RT(587–596 SF2) EPIVGAETF HIV-1 infection human(B35, B51) [Shiga (1996)]

- Binds HLA-B*3501, and is also presented by B51 – but CTL could not kill RT-vaccinia virus infected cells that expressed B51

RT(432–440) Pol(587–595) EPIVGAETF HIV-1 infection human(B35, B51) [Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al.* as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

---

RT(432–441) Pol(587–596) EPIVGAETFY HIV-1 infection human(B*3501) [Tomiyama (2000a)]

- CD8+ T-cells that bound one of six HIV-specific B*3501-epitope tetramers did not express CD28 or CD45A
- A significant increase in CD28-CD45RA- cells and a decrease of CD28+CD45RA+ cells was observed in chronically HIV-1-infected individuals relative to healthy individuals
- CD28-CD45RA- cells are likely to be effector cells and have high levels of perforin in their cytoplasm
- The mean percentage of total CD28- CD8+ cells in chronically infected HIV-1-infected patients was 76.6% in comparison to HIV-1-uninfected individuals (40.6%)

RT(432–441)	RT(587–597 SF2)	EPIVGAETFY	HIV-1 infection	C3H/HeJ mice(B35)	[Menendez-Arias (1998), Shiga (1996)]

- Binds HLA-B*3501, but not presented by B51, in contrast to the peptide EPIVGAETF
- [Menendez-Arias (1998)] note in their review that this epitope is located near the protease cleavage site and conservation of this region is important for viral maturation
- This epitope spans the Pol p66 RT – p15 (RNAse) domain

RT(432–441)	RT(587–597 SF2)	EPIVGAETFY	HIV-1 infection	human(B35)	[Kawana (1999)]

- HLA B35 is associated with rapid disease progression
- The sequences of 9 previously described HIV-1 B35 CTL epitopes were obtained in 10 HLA B35+ and 19 HLA B35- individuals
- 3/9 CTL epitopes had substitutions that were more common in B35+ individuals than in B35- individuals, but this was one of the six that had no B35 associated pattern of mutation

RT(434–447)	RT( )	IVGAETFYVDGAAS	HIV-1 infection	human(A*6802)	[Menendez-Arias (1998), van der Burg (1997)]

- Recognized by CTL from a long-term survivor that recognized a set of 5 overlapping peptides spanning IVGAETFYVDGAAS as well as PIVLPEKDSW and KITTESIVIW
- A*6802 is a subset of HLA-A28
- This epitope spans the Pol p66 RT – p15 (RNAse) domain

RT(436–445)	RT(591–600 IIIB)	GAETFYVDGA	HIV-1 infection	human(B45)	[Menendez-Arias (1998)]

- This epitope spans the Pol p66 RT – p15 (RNAse) domain

RT(436–445)	Pol(591–600 IIIB)	GVETFYVDGA	HIV-1 infection	human(B45)	[Wilson (1999a)]

- This study describes maternal CTL responses in the context of mother-to-infant transmission
- Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants
- No variants of this epitope were found in a non-transmitting mother who had a CTL response to it
- This epitope spans the Pol p66 RT – p15 (RNAse) domain

RT(437–445)	Pol(592–600 HXB2)	AETFYVDGA	HIV-1 infection	human(B*4501)	[Mulligan (2001)]

- Epitope P59 from Patient 07107 with HLA genotypes A*3002, A*3201, B*4501, B*5301, Cw*0401, Cw*1202

RT(437–447)	RT(592–602 LAI)	AETFYVDGAAN		human(A28)	[Brander & Walker(1996), Menendez-Arias (1998)]

- P. Johnson, pers. comm.
- This epitope spans the Pol p66 RT – p15 (RNAse) domain

RT(437–447)	Pol(592–602)	AETFYVDGAAN	HIV-1 infection	human(A28)	[Ferrari (2000)]

- One of the 51 HIV-1 epitopes selected by Ferrari *et al*. as good candidate CTL epitopes for vaccines by virtue of being conserved and presented by common HLA alleles

RT(438–448)	RT(593–603 IIIB)	ETFYVDGAANR	HIV-1 infection	human(A26)	[Menendez-Arias (1998)]
	• This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT(438–448)	Pol(593–603 IIIB)	ETFYVDGAANR	HIV-1 infection	human(A26)	[Wilson (1999a)]
	• This study describes maternal CTL responses in the context of mother-to-infant transmission • Detection of CTL escape mutants in the mother was associated with transmission, but the CTL-susceptible forms of the virus tended to be found in infected infants • One other variant was found that gave a positive, though reduced, CTL response: ETYYVNGAANR • This epitope spans the Pol p66 RT – p15 (RNAse) domain				
RT(448–457)	RT( )	RETKLGKAGY	HIV-1 infection	human(A29)	[van der Burg (1997)]
	• Patients studied were from the Amsterdam cohort • CTL epitopes of 3 rapid progressors were compared to 4 long-term survivors (LTS) and no differences could be found in the degree of conservation in the two groups • Epitope recognized by an LTS • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(449–457)	Pol(604–612 HXB2)	ETKLGKAGY	HIV-1 infection	human(A*2601)	[Mulligan (2001)]
	• Epitope P61 from Patient 02112 with HLA genotypes A*3303, A*2601, B*5801, B*8201, Cw*0302, Cw*07(01, 06) • Epitope P61 Patient 02112 has an other optimal peptide N11, DILDLWIF with HLA Cw*0701 and Cw*0706				
RT(481–505)	RT(648–672)	AIYLALQDSGLEVNIV-TDSQYALGI	HIV-1 infection	human( )	[Menendez-Arias (1998), Price (1995)]
	• Study of cytokines released by HIV-1 specific activated CTL • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(481–505)	RT(648–672 PV22)	AIYLALQDSGLEVNIV-TDSQYALGI	HIV-1 infection	human(B14)	[Kalams (1994), Menendez-Arias (1998)]
	• A CTL response used to study gene usage in HLA-B14 response • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(485–493)	RT(640–648 HXB2R)	ALQDSGLEV	Vaccine	human(A2)	[Brander (1995)]
	Vaccine: *Strain:* HXB2 *HIV component:* RT • Epitope studied in the context of inclusion in a synthetic vaccine • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(485–493)	RT(640–648 HXB2R)	ALQDSGLEV	HIV-1 infection	human(A2.1)	[Brander (1995), Brander (1996)]
	• This epitope was recognized by PBMC from 3/14 HIV+ asymptomatic patients				

- This epitope was used along with Env CTL epitope TLTSCNTSV and a tetanus toxin T helper epitope for a synthetic vaccine
- This vaccine failed to induce a CTL response, although a helper response was evident
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT

RT(485–505) RT(648–672) ALQDSGLEVVTDSQY-ALGI HIV-1 infection human(B14) [Brander & Walker(1995)]

- Unpublished, S. Kalams
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT

RT(496–504) Pol(651–659 HXB2) VTDSQYALG HIV-1 infection human(B*1503) [Mulligan (2001)]

- Epitope P66 from Patient 03115 with HLA genotypes A*3002, A*68(011, 08), B*0801, B*1503, Cw*07(01, 06), Cw*08(02, 05)

RT(496–505) Pol( ) VTDSQYALGI HIV-1 exposed seronegative human(B14, B*1402) [Rowland-Jones (1998b)]

- HIV-specific CTL were found in exposed seronegative prostitutes from Nairobi – these CTL may confer protection
- Seroprevalence in this cohort is 90-95% and their HIV-1 exposure is among the highest in the world
- Most isolated HIV strains are clade A in Nairobi, although clades C and D are also found – B clade epitopes are often cross-reactive, however stronger responses are frequently observed using A or D clade versions of epitopes
- This epitope is conserved among A, B and D clade viruses

RT(496–505) RT(663–672 IIIB) VTDSQYALGI HIV-1 infection human(Cw8) [Brander & Walker(1996)]

- Unpublished, P. Johnson
- Published in this database in 1995 as B14, but B14 transfected cells did not present the peptide and it is thought to be presented by the genetically linked Cw8 molecule instead [Brander & Walker(1996)]
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT

RT(496–505) RT( ) VTDSQYALGI HIV-1 exposed seronegative human(Cw8) [Rowland-Jones (1998a)]

- A CTL response was found in exposed but uninfected prostitutes from Nairobi using previously-defined B clade epitopes that tended to be conserved in A and D clades – such cross-reactivity could protect against both A and D and confer protection in Nairobi where both subtypes are circulating
- The A and D subtype consensus are identical to the B clade epitope
- Thought to be HLA-Cw8 restricted, not B14 as originally reported (C. Brander, B. Walker, and S. Rowland-Jones, personal communication)
- This epitope occurs in the p15 (RNAse) domain of Pol p66 RT

RT(509–518) Pol( ) QPDKSESELV human(B7) [De Groot (2001)]

- The program Epimatrix was used in conjunction with the program Conservatrix to identify conserved regions of HIV that might serve as epitopes
- A subset of the potential epitopes was identified that could bind to the appropriate HLA-allele, and 15 predicted B7 superfamily (HLA B7, B8, and B58) epitopes were identified that could stimulate IFNγ production in an ELISPOT assay
- QPDKSESELV was newly identified as an HLA-B7 epitope in this study

---

RT(516–525)	RT(516–525)	ELVNQIIEQL	HIV-1 infection	human(A2)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				
RT(520–528)	Pol(520–528 LAI)	QIIEQLIKK		human(A*1101)	[Brander & Goulder(2001), Fukada (1999)]
	• C. Brander notes this is an A*1101 epitope				
RT(530–538)	Pol(685–693 HXB2)	KVYLAWVPA	HIV-1 infection	human(A*0301)	[Mulligan (2001)]
	• Epitope P69 from Patient 07124 with HLA genotypes A*0202, A*0301, B*4501, B*5301, Cw*1502, Cw*0401				
RT(532–540)	Pol(714–722)	YLAWVPAHK	HIV-1 infection	human(A3 supertype)	[Propato (2001)]
	• Long-term non-progressors (LTNPs) had strong memory resting CD8+ T-cell responses against the majority of epitopes tested (18 for the A2 supertype, 16 for the A3 supertype) while the effector cells of long-term non-progressors recognized far fewer epitopes • Progressors had memory resting CD8+ T-cells that recognized far fewer epitopes than LTNPs • A positive correlation between effector CD8+ T-cells and plasma viremia and a negative correlation between CD8+ effector T-cells and CD4+ T-cells was observed, which may contribute to the inability of LTNPs to clear virus • This epitope can bind 5/5 HLA-A3 supertype alleles (A*0301, A*1101, A*3101, A*3301 and A*6801)				
RT(532–540)	RT(532–540)	YLAWVPAHK	HIV-1 infection	human(B7)	[Haas (1998)]
	• Of 98 patients in cross-sectional analysis, 78% had CTL against pol – RT was more immunogenic than Integrase and Protease (81%, 51%, and 24% of 37 patients, respectively) • New clusters of epitopes were defined utilizing different HLA molecules • This epitope occurs in the p15 (RNAse) domain of Pol p66 RT				